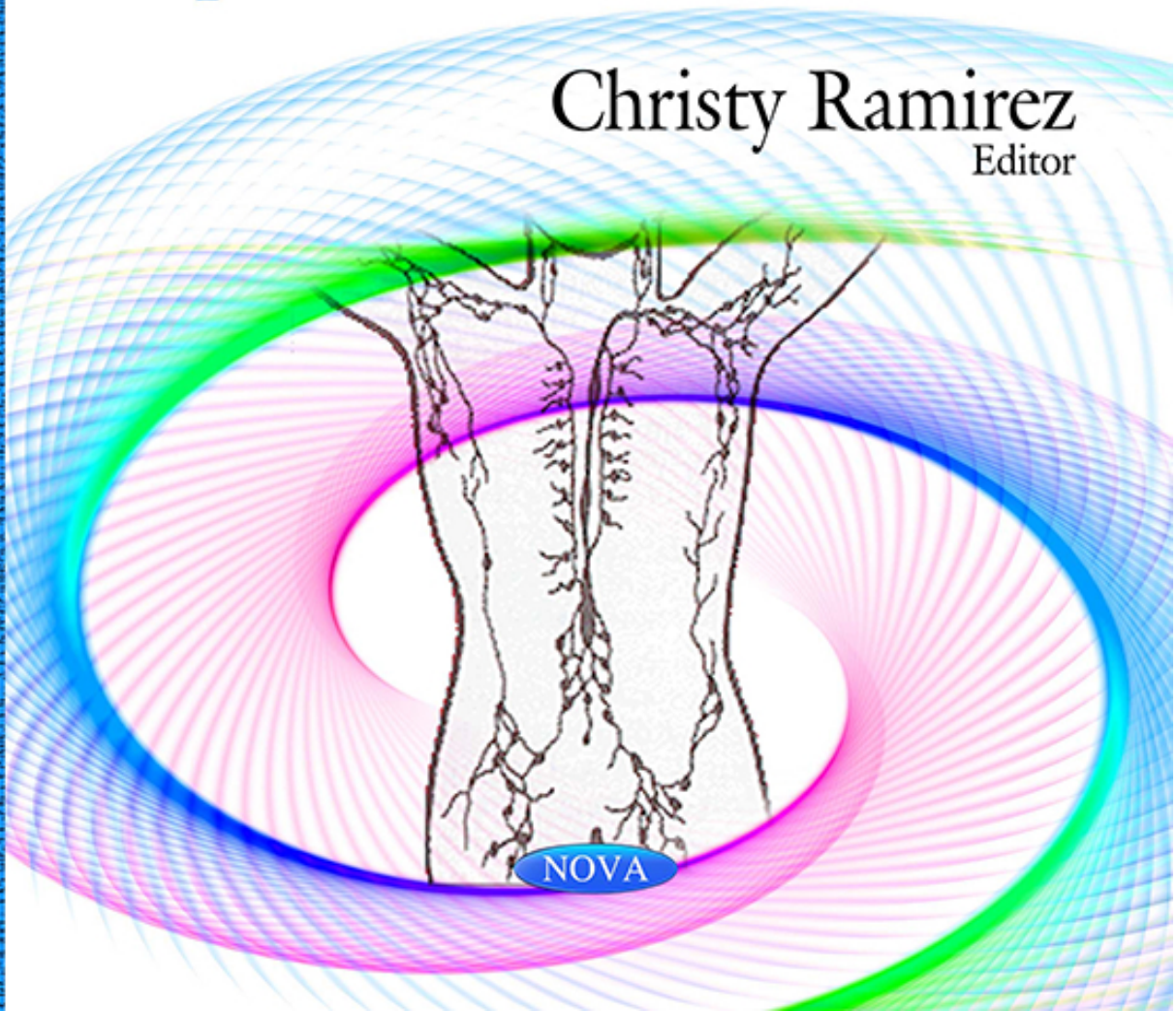
HUMAN ANATOMY AND PHYSIOLOGY

The Lymphatic System

Components, Functions and Diseases

Christy Ramirez
Editor



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THE LYMPHATIC SYSTEM

COMPONENTS, FUNCTIONS AND DISEASES

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CHRISTY RAMIREZ
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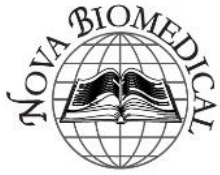

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PREFACE

This book provides research on the components, functions and diseases of the lymphatic system. Chapter One reviews the role of lymphatic drainage of cerebrospinal fluid from the brain. In particular, the authors review the current hypotheses on the possible drainage of lymphatic fluid from the brain. Chapter Two expose the actual refinements of the surgical technique for the pedicled and free greater omentum flap, facing the treatment lymphedema. Chapter Three summarizes the recent development of the molecular mechanisms of tumor lymphangiogenesis, especially the role of bone marrow-derived cells and the growth factors implicated in this process. Chapter Four reviews molecular mechanisms related to the activation of tumor lymphangiogenesis and their clinical implications.

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Chapter 1

CEREBROSPINAL FLUID CIRCULATION: BRAIN LYMPHATICS, BRAIN GLYMPHATICS, OR BOTH?

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ABSTRACT

We briefly review the role of lymphatic drainage of cerebrospinal fluid from the brain. In particular, we review the current hypotheses on the possible drainage of lymphatic fluid from the brain. The intriguing point is that although lymphatics are absent in the brain, a very complex brain-wide paravascular pathway for cerebrospinal fluid and interstitial fluid exchange is present which allows efficient clearance of solutes and

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waste from the brain. The role of cervical lymphatic vessels is critical and various models describing the anatomical connection between the subarachnoid space and the nasal lymphatic vessels are discussed.

Keywords: brain lymphatic system, brain glymphatic system, cervical lymphatic vessels

BASIC CONCEPTS

Extra-cellular fluid is generated through filtration in most tissues. Filtration occurs when the hydrostatic pressure in the capillary exceeds the opposing force represented by the intra-vascular colloid osmotic pressure of the plasma proteins. The resulting interstitial fluid (ISF), which contains proteins, solutes, and waste substances from the metabolism of the various tissues, is drained through the lymphatic system and eventually returns into the blood. Hence, the role of the lymphatic network, which is ubiquitous in the human body, is to filter the cellular waste out of circulating fluids throughout the organism. In this scenario, the brain represents an amazing exception, since it is completely devoid of lymphatics. This is very unusual, considering that the brain is certainly an energy hog and can falter as soon as its metabolism gives the slightest sign of unbalance.

Although scientists have believed for years that cerebrospinal fluid (CSF) acts as the brain's highly refined lymphatic system, two statements are traditionally very difficult to link: as reported above, there are no lymphatic vessels in the brain parenchyma and there is a highly specialized system that allows the CSF to move into the brain, thus replacing fluid inside the brain. An old study by Schwalbe (1869) [1] which involved injecting Berlin Blue dye into the subarachnoid space in dogs demonstrated that the lymphatic system is the main clearing outlet for CSF. This hypothesis was reviewed and discussed repeatedly after its publication. The role of the lymphatic system in the drainage of proteins in case of hemorrhage or infection has been reviewed as well [2, 3]. It has been known since 1872 [4] that there is indeed a circulatory exit pathway of CSF through the arachnoid granulations into lymphatic vessels in the nasal mucosa, the frontal sinus and along cranial nerves. Several articles support this hypothesis describing experiments performed in different species [5]. This lymph draining pathway, which runs through the olfactory tracts, passes across the cribriform plate (lamina cribrosa) and the nasal mucosa and reaches the retropharyngeal lymph-nodes and, eventually, the nodes at the base

of the neck, was found to be present also in the human body [5]. However, lymphatic drainage may alternatively – or rather, in addition - occur also through nerve pathways other than the cribiform plate, such as the optic, auditory, trigeminal, or facial nerves, as well as through other cranial and lumbar spinal nerves [5].

The extracellular fluid compartment of the brain is usually divided into two components, i.e., CSF and parenchymal ISF [6]. The most widely accepted theory is that CSF is mainly secreted by the four choroid plexuses (CPs) within the brain ventricles, then it flows inside the ventricular cavities and reaches the subarachnoid spaces (through the Luschka and Magendie foramina), after which it is mainly conveyed into venous sinuses through the arachnoid villi (Pacchioni granules). As for the parenchymal ISF, this is thought to be actively secreted by the capillary endothelial cells; it then moves to the capillary glial complex through the perivascular and subependymal regions into the ventricular system and subarachnoid space, where it mixes with the CSF [7].

This hypothetical model has been widely discussed and criticized on the basis of results obtained from *"in vivo*" studies, leading to the belief that there is little evidence to continue supporting it [5].

Cerebral spinal fluid is mainly produced by the choroid plexuses which are made up of infoldings of blood vessels covered by a thin tissue called pia and are located in the four ventricles of the brain – the largest of which are found in the lateral ventricles. The CSF flows or communicates between the lateral ventricles and the third ventricle through the interventricular foramen (also called the foramen of Monro). The cerebral spinal fluid then slowly flows from the third ventricle to the fourth ventricle through the aqueduct of Sylvius. From the fourth ventricle, the CSF then passes through the foramen of Luschka and the foramen of Magendie, after which it enters the subarachnoid space that externally bathes the cerebral structures of the brain and spinal cord. Flowing along the subarachnoid cisterns, the CSF is then reabsorbed by the arachnoid granulations (also called the granulations of Pacchioni) that are mainly distributed along the superior sagittal sinus.

In this chapter we would like to briefly review what is now known about this fascinating field and to show experimental evidence that CSF runs into the brain as scientists have indeed, long believed, but that an incredibly advanced network of anatomical structures, a kind of non-conventional "*brain hyper-lymphatic highway system*," allows CSF circulation and brain cellular waste filtering. Finally, in the framework of this still ill-defined mechanism, we will address the fascinating conundrum represented by the human fetus.

CSF PRODUCTION

The concepts of CSF production and reabsorption are shown in Figure 1. Although there is general agreement that CSF is produced mainly by CPs, two different mechanisms are claimed to be in place for its production. In the first, passive plasma filtration driven by hydrostatic pressure is thought to occur through the fenestrated choroidal capillary endothelium with the CSF flowing from the basolateral surface towards the apical surface [8]. The second hypothesis states that there is active secretion through the apical surface of the choroidal epithelium, with a very limited, if non-existent, role played by hydrostatic or oncotic pressures [9]. The ventricular ependyma has also rarely been reported as a possible additional source of CSF production [5]. Considering the existence of a transmantle pressure gradient, i.e., the difference between the pressure inside the brain ventricular system and that in the subarachnoid spaces, it has been suggested that CPs are not the main organs responsible for CSF production, thus casting serious doubts on the classic model of CSF production [11-14]. According to these recent experimental studies, the ISF, i.e., the fluid within the cerebral parenchyma, and the CSF, i.e., the fluid in the sub-arachnoid spaces, would constitute a functional unit whose main regulatory factors are represented by the osmotic and hydrostatic pressure in the capillaries and the IF-CSF unit (Figure 1).

It must be kept in mind that there are differences between fluid transport across peripheral and cerebral microvessels. In peripheral microvessels, water can pass both through and between the cells, while in cerebral microvessels water can only pass through the cells due to the presence of tight junctions. Net water movement and small solute diffusion are the result of hydrostatic and colloid osmotic pressure differences between blood and tissues in the first case, while in the second case the movement of small solutes and water is impaired, thus requiring the action of specific transports.

CSF (RE) ABSORPTION AND THE FETAL CONUNDRUM

CPs would appear to be able to reabsorb about 1/10th of their own secretion, making them similar to the proximal renal tubule [15]. Arachnoid villi granulations (AVG) act as accessory reabsorptive pathways; this is true even under conditions of elevated CSF pressure, wherein the AVG reabsorption rate remains limited [16]. Arachnoid granulations are poorly

formed and non-functional in utero; they are present as villi in the late third trimester, as granulations at 39 weeks, and become fully functional somewhat further on, thus making the possibility that one or more alternative reabsorption mechanisms must exist quite feasible. Extra-cranial lymphatic vessels certainly play a key role in regulating CSF balance during intrauterine life and - most likely - neonatal age too, even if this cannot be the sole mechanism involved.

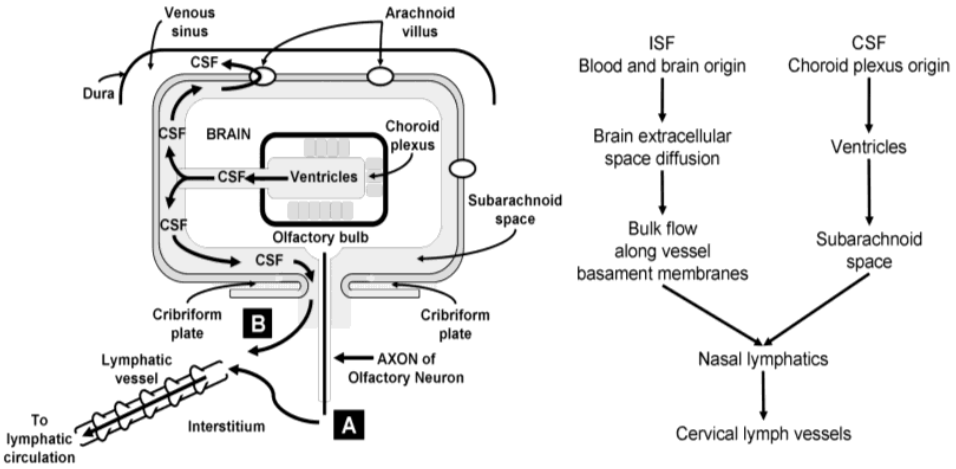

Figure 1. Diagram showing the separate pathways of lymphatic drainage of cerebrospinal fluid (CSF) from the brain. Traditional CSF secretion, transport, and reabsorption.

There is general consensus that the bulk flow of CSF occurs through arachnoid projections into the cranial and spinal venous systems [17] (Figure 1). First identified by Pacchioni in the 18th century, the microscopic arachnoid villi and the macroscopic arachnoid granulations represent herniations of the cranial arachnoid membrane projecting into the venous sinuses of the dura mater on the convexity of the brain. Absorption is driven by the differences in hydrostatic pressure between the CSF compartment and the venous system. Mechanisms of CSF transport are still under debate. Active phagocytosis, pressure-dependent pinocytosis, vacuoles, transcellular channels, gaps between cells of the endothelium surrounding the venous sinus, and passive transport via extracellular cisterns are all possible mechanisms which are believed to be involved in CSF transport [5]. Many questions are still open, and a definitive pathway explaining the precise role of AVG in CSF absorption has not yet been discovered [5]. CPs develop early in gestation, filling both lateral ventricles during the third month of gestation, confirming

that these anatomic structures are highly involved in CSF production and that the fetus needs other ways to reabsorb CSF, thus maintaining the equilibrium between production and reabsorption.

EXTRA-CRANIAL LYMPHATIC VESSEL ORGANIZATION AND ROLE

The concept of CSF transport into cervical lymphatic vessels and the various hypothetical anatomical architectures are illustrated in Figure 2.

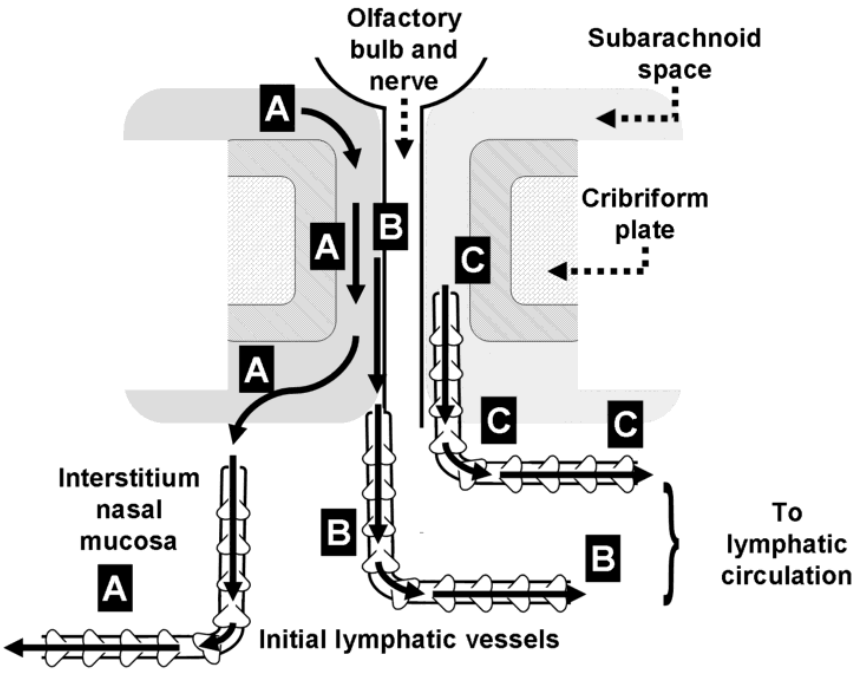

Figure 2. The perineural lymphatic pathway of cerebrospinal fluid drainage. The concept of CSF transport into cervical lymphatic vessels and the various possible anatomical architectures. Different models describe the anatomical connection between the subarachnoid space and the nasal lymphatic vessels. A. The subarachnoid space extends along the nerve to the nasal mucosa, thus causing the CSF to leak into the nasal mucosa and to enter the initial cervical lymphatic vessels. B. The subarachnoid space connects to the perineural space of the olfactory nerves. The perineural space then reaches the nasal mucosa and spreads into the interstitial tissue of the nasal mucosa, thus entering the lymphatic vessels. C. The subarachnoid space is present along the olfactory nerves in the cribriform plate, and connects directly with the lymphatic vessels of the nasal mucosa. This option may be considered a variant of the B option.

As reported above, no lymphatics exist in the brain parenchyma. In particular, it has long been [18] known that lymphatics are indeed present in several endocranial tissues, such as dura mater, pia mater, pituitary capsule, orbits, middle ear, and, above all, nasal mucosa [19] but not in the brain parenchyma itself. This archiceture does not provide adequate waste drainage from the highly performant and metabolically active adult brain, let alone the hypermetabolically active fetal one. Despite the fact that a physiological association between extra-cellular cerebral fluid and extra-cranial lymph has been known for over 100 years, this concept has never been thoroughly embraced by the biomedical community. An active role of the lymphatics in the drainage of the brain extra-cellular fluid was suggested for the first time in 1869 [1] and strongly supported only almost a century later [5]. The timeline of landmark publications in CSF outflow and in the lymphatic pathway of CSF drainage was extensively reviewed by Kapoora in 2008 [19]. The presence of lymphatic pathways related to CSF outflow was hypothesized by Weed in 1914 [20]. It was then demonstrated that lymphatics manage roughly 50% of the whole CSF absorption and that their activity increases in the presence of an increase in intra-ventricular pressure, so that the contribution of the arachnoid villi remains stable at roughly 50% [21]. Experimental evidence demonstrated that protein tracers injected in the CSF or into the brain interstitium can exit the brain via cranial lymphatic vessels located along the perineural space of cranial nerves crossing - in particular - the cribiform plate, although other potential locations leading CSF access to cervical lymphatic vessels cannot be excluded [5]. The cribiform plate – which is located at the base of the skull - supports the olfactory bulb. The axons of the olfactory nerves pass through the small holes of the cribiform plate and reach the olfactory epithelium in the nasal mucosa, thus connecting with the lymphatic vessels of the mucosa [15, 19]. Various models have been proposed to describe the anatomical connection between the subarachnoid space and the nasal lymphatic vessels (Figure 2). Some older papers reporting methods that can separate and quantitate CSF tracer clearance through arachnoid villi and extra-cranial lymphatic vessels in both sheep and rat models demonstrated that cervical lymphatics participate in the removal of endocranial CSF, whereas lymphatics leading to lumbar nodes receive spinal CSF.

In general, it is very difficult to correctly quantitate the lymphatic contribution to CSF absorption both in animal models and, even more so, in humans. Cannulating all cervical lymphatics and evaluating the role of the right lymph duct in animal experimental models remains a challenge; we can only imagine that the role of lymphatics in CSF absorption might be even

greater than currently thought. In 1997, Brinker et al. [22] hypothesized that CSF may exit the peri-neurial sheaths and flow into the extracellular space, although the mechanisms of lymphatic absorption are still poorly understood. CSF circulates within the subarachnoid space enclosed by the perineurial shealth. Figure 3 shows both the open-cuffed and the closed cuffed model for CSF lymphatic drainage through the perineurial sheath [19].

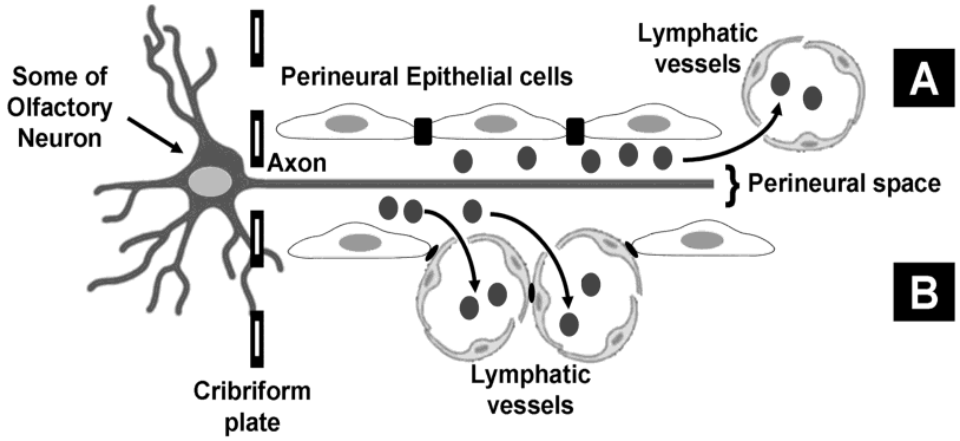

Figure 3. A schematic illustration of the two main routes the perineural space that can be followed by the tracers in the CSF to reach the lymphatic system. A may be defined open-cuff model, whereas B describes a closed-cuff model. You may imagine that the lymphatic vessels form a sort of sealing collar.

Previous observations [23] supported the hypothesis that lymphangiogenesis plays an important role in nuchal edema since increased nuchal translucency may be related to a developmental delay of the lymphatic system. It is possible to speculate that in the presence of increased nuchal translucency, delayed or disturbed development of the fetal lymphatics of the cervical region may trigger a reduction in the drainage of CSF via the perineural space through the cribiform plate.

BRAIN INTERSTITIAL DRAINAGE: GLYMPHATICS

Considering that the brain lacks a lymphatic network and circulation, cerebral extracellular proteins and waste must be cleared through alternative mechanisms. Recently, several authors [24-27] described an alternative system, which they named the glymphatic system. This represents a brain-wide, paravascular pathway for CSF and ISF exchange which results in the

efficient clearance of solutes and waste from the brain. Figure 4 shows a schematic drawing of the glymphatic system and its relationship with lymphatic vessels. Two very recent studies [27, 28] demonstrated the presence of a complex brain pathway involved in both the exchange of CSF and ISF, and in the clearance of interstitial solute from the brain. According to Iliff et al. [27], who first described this important pathway, it consists of a para-arterial CSF influx route, a para-venous ISF clearance route, and a transparenchymal pathway that is dependent on astroglial water transport via the astrocytic aquaporin-4 (AQP4) water channel.

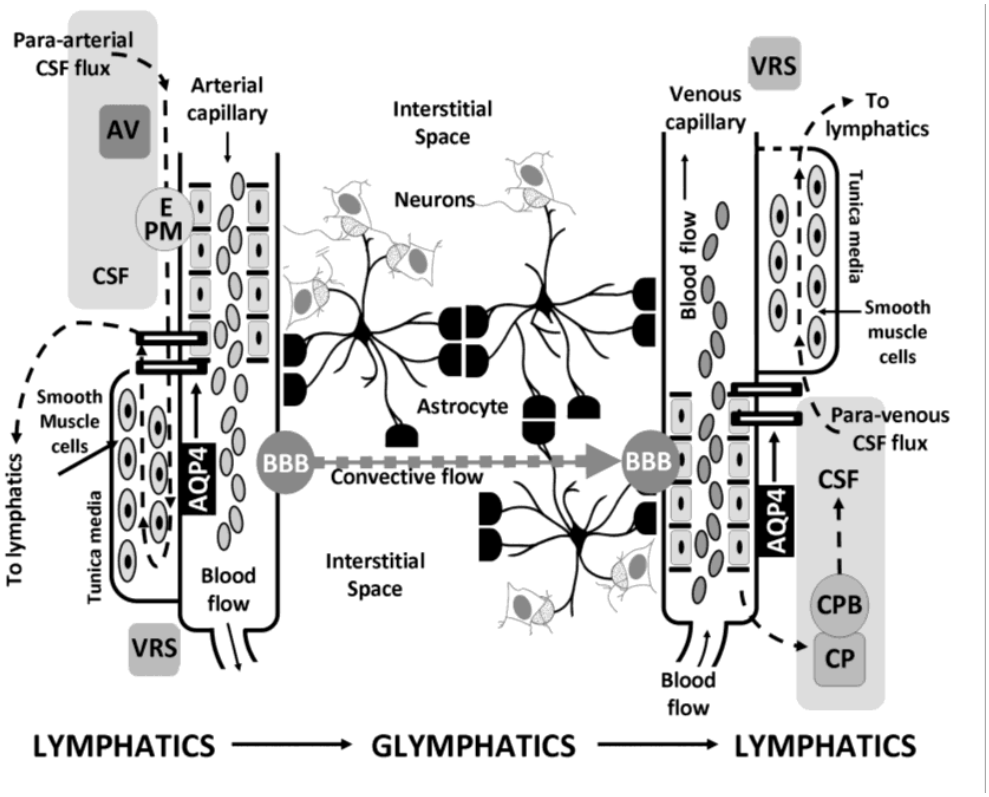

Figure 4. Schematic of brain glymphatic pathway function. CSF from the subarachnoid space rapidly enters the brain along the para-arterial channels surrounding the penetrating arteries and exchanges with brain interstitial fluid (ISF). ISF and solutes are cleared to the paravascular spaces surrounding large caliber draining veins. Convective bulk fluid flow between the paravascular CSF influx and ISF efflux pathways is facilitated by astroglial water transport through aquaporin-4. AV: Arachnoid villus; BBB: Blood-Brain barrier; EPM: Ependyma Pia Mater; VRS: Virchow-Robin Space; CP: Choroid Plexus; AQP4: aquaporin-4; CPB: Choroid Plexus barrier.

CONCLUSION

Fluid is secreted into the CSF by the CPs and into ISF at the level of the blood-brain-barrier (BBB). Secretion is an active process linked to Na^+, K^+-ATPase, and the Na^+-pump. An intact BBB cannot reabsorb fluid. Fluid can return to lymph and blood by a perineural pathway leading to the olfactory epithelium and the AVGs. The secretion rates between CPs and BBB are largely uncertain.

Significant volumes of CSF drainage into the extracranial lymphatic vessels has generally been ignored, even though an association between CSF and lymph has long been known. CSF mainly flows along the extensions of the subarachnoid compartment associated primarily with olfactory nerves, then it passes through the cribriform plate and is eventually drained by lymphatics into the nasal submucosa. Over the last few years, interest in cerebral lymphatics has increased, and recent, interesting studies have demonstrated that the waste cerebral system is a truly complex structure and a highly advanced lymphatic system. The recent attention that has been directed to lymphatic CSF absorption may reveal new insights into the cause of CSF disorders and provide novel targets for therapeutic intervention.

In this scenario, the fetal model is indeed intriguing because as mentioned before, Pacchioni arachnoid granules are not fully efficent before birth. If this is true, as it is, then the next question must be "How does the fetal brain get rid of its waste and extra-cellular fluid?" It has been hypothesized that the answer to this question lies in the existence of glymphatics in the fetus. In fact, if we speculate that there is a yet to be discovered path linking CSF, extra-cellular fluid and cervical lymph nodes, then why do fetuses with delayed or abnormal development of this cervical lymphatic network (such as those with enlarged Nuchal Translucency or cystic hygroma in the 1st trimester) not show dilatation of the ventricular system? This challenging field of research is still open and appealing, as is demonstrated by the recent publication of interesting and suggestive articles [29-35].

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Chapter 2

VERSATILITY AND INNOVATIONS OF THE GREATER OMENTAL FLAP IN THE SURGICAL TREATMENT OF LYMPHEDEMA OF THE UPPER AND LOWER LIMBS

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ABSTRACT

Lymphedema is a cronic debilitating disease affecting a considerable part of the population that results from impairment of the lymphatic system. This is highly prevalent in patients subjected to axillar nodal dissection after breast oncologic surgery, surgery of the abdominopelvic area, axilar or groin lymphadenectomy after melanoma or radiotherapy in the mentioned areas. Interestingly lymph node transfer proceeding from

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the groin has been the initial indication in the surgical treatment of lymphedema, but unfortunately a significant morbidity can be produced at the donor site that may lead to a new iatrogenic lymphedema. For this reason, new donor nodal groups are being used, like the ones located at the submental and supraclavicular areas. The greater omentum is also a current and efficient donor site of lymph nodes and lymphatic vessels. Dissection of the omentum is easy to perform and can be done even in patients who had previous abdominal surgeries. In this chapter we will expose the actual refinements of the surgical technique for the pedicled and free greater omentum flap, facing the treatment lymphedema. Data regarding the vascular anatomy and the distribution of lymph nodes and lymphatic vessels in the greater omentum will be included.

INTRODUCTION

Lymphedema is a cronic debilitating disease affecting a considerable part of the population that results from impairment of the lymphatic system. It is known that each lymph node has afferent lymphatic vessels that transport lymph and an efferent system that transports fluid toward the thoracic duct. Lack of coordination among arterial inflow, venous outflow, and osmotic forces acting within the tissues may contribute to the development of lymphedema.

This pathology is highly prevalent in patients when axillary node dissection has been performed, specially after breast oncologic surgery with or without radiotherapy and even after sentinel node biopsy, but also when this nodal surgery or radiotherapy has been practiced in the abdominopelvic area. Despite the fact that sentinel node biopsy has reduced the incidence of lymphedema [1], this is still a complication that produces a negative impact in the patients and in the sanitary system.

In recent years the surgery of lymphedema was reactivated since Professor Koshima introduced the term supermicrosurgery [2, 3, 4, 5]. His works opened a door that encouraged many other surgeons to follow his efforts. Thank to this, there has been an evolution of surgical techniques that make possible an improvement of the lymphedema affecting limbs but also the craniofacial area. Also those cases that were established years before can be candidates to surgery.

Two main surgical techniques are accepted today as the goal standard for the surgery of lymphedema: vascularized lymph node transfer (VLNT) and lymphovenous anastomosis (LVA). The application of one or another depends

on the degree of lymphedema, time of evolution and experience of the surgical team, but otherwise both procedures have shown to be effective. On the other hand, they can be performed at the same time if needed, or be a complementary technique if one of them has been insufficient to obtain a satisfactory result.

VLNT is currently a popular technique for the surgical treatment of lymphedema. Microvascular transfer of a single group of lymph nodes is the most common procedure in the clinical practice but also groups of lymph nodes associated to microvascular flaps like the DIEP (deep inferior epigastric perforator) flap can be transferred simultaneously to perform a total breast reconstruction and to improve the secondary lymphedema.

The concern associated with VLNT is based on the possibility of causing irreversible damages in the donor zone which may lead to a significant alteration of the lymphatic drainage. This fact may cause another lymphedema in a different anatomical area which is a devastating complication. For this reason, different donor areas of lymph nodes have been proposed lately, like the submental and the supraclavicular ones [6, 7].

The greater omentum (GO) has shown to be an excellent donor site of lymphatic tissue and is an alternative to the previously mentioned nodal groups [8]. Omentum dissection can be done by laparotomy or by laparoscopy, even in patients who had previous abdominal surgeries. In this chapter anatomical aspects regarding the lymphatic system of the greater omentum will be showed as well as surgical details that have to be applied when the greater omentum is used to perform a surgical treatment of the lymphedema.

VASCULARIZED LYMPH NODES TRANSFER IN THE SURGICAL TREATMENT OF LYMPHEDEMA

VLNT is one the most important and demanded surgical technique for lymphedema treatment. Today it is possible to transfer this tissue into a swollen limb in which there is a reduced lymph discharge by means of new microsurgical procedures, and obtain an improvement in the circulation of the lymph.

As capillary angiogenesis has been demonstrated in lymphedema and also lymphangiogenesis in postmastectomy patients, we can speculate that vascularized lymph nodes transfer promotes long-term lymphangiogenesis that improves lymphatic clearance of the deep lymphatic drainage acting as a

lymphatic pump [9, 10], in relation to the robust regenerative capacity of the lymphatic vessels [11]. On the other hand it has been published that cutaneous collateral lymphatic channels are important in rerouting lymph along a dermal pathway in the swollen limb [12, 13].

Therefore restoration of lymph nodes function requires establishment of adequate perfusion. Due to its size, when doing lymph node transfer, large arteries and veins that irrigate the group must be dissected, to be sure that we can transplant those groups of nodes as a vascularized system.

Vascularized groin lymph nodes have been transferred to the axilla after postmastectomy lymphedema [14, 15] and indeed some authors stated that it is the most physiological method to restore the afferent lymphatic pathways and deliver the lymph load to the deep venous system [16, 17].

The groin region has been the favourite anatomical area to harvest vascularized lymph nodes [18, 19] when the initial series were described in the medical literature. Groin lymph nodes are classified into deep and superficial groups. However, the vascular anatomy presents numerous variations that have been associated to flap failure. According to this Acland, Cormack and Lamberty stated that the superficial branch of the circumflex iliac artery is the main supply of the lymph nodes in the groin [20, 21].

The negative point when dissecting groin lymph nodes lays in the undesired possibility of producing a lesion of the lymphatic system that can lead to iatrogenic lymphedema in the lower limb. For this reason different donor zones are being used lately to obtain functional vascularized lymph nodes, like submental or supraclavicular areas [6, 7]. They seem to produce lesser iatrogenic secuelae after dissection and the flaps can be designed with or without a skin paddle. Otherwise, preoperative ultrasound is a valuable and recommended tool to study the number of lymph nodes and its location prior to flap harvest. Nevertheless, fatal complications after harvesting these flaps exist, like paralisis of the marginal branch of the facial nerve.

On the other hand, microsurgical LVA has a place today in the treatment of peripheral lymphedema, being also a choice for patients who are not sufficiently responsive to non surgical treatment [22, 23]. Despite VLNT and LVA showed to be effective, some authors still think that there is a minimal reduction in volume of lymphedema following supermicrosurgical techniques [24]. These ones conclude that non-operative treatment and elastic stockings are still preferred by most patients with lymphedema, especially in early stages with few irreversible changes. In fact both procedures seem to be complementary in real practice [25].

REGIONAL ANATOMY OF THE GREATER OMENTUM

GO is a large peritoneal fold consisting of connective tissue, fat and lymphatics. It is well vascularized with large feeding arteries and draining veins. Previous abdominal surgery may render the omentum scarred and adherent to the intra-abdominal contents, and therefore may preclude its use. Because harvesting may require laparotomy this flap is used infrequently, but nowadays it is getting more and more popular, especially when laparoscopic harvesting is performed.

GO is often referred to by the surgeons as the abdominal policeman. The lower, right and left margins are free, which allows movements about the peritoneal cavity in response to the peristaltic movements of the neighboring gut.

Understanding of the vascular anatomy of the omental vascular arcade is crucial to the concept of greater omentum flap harvesting. The right and the left gastroepiploic vessels and their panches along the greater curvature of the stomach form the omental vascular arcade. The panches consist of the right and left omental artery, the middle omental artery, the accessory omental artery and short omental arteries. The middle omental artery, which is the major panch further, divides into right and left panch which join the right and left omental arteries. The presence of this omental arcade allows the omentum to be lengthened as far as down the ankle by division of the side panches basing the pedicle on the right or the left gastroepiploic artery.

Alday and Goldsmith [26] performed autopsy studies on 136 adult cadavers and described five types of omental vascular arcades depending upon the level of bifurcation or the absence of the middle omental artery. Type 1 is most common and involves bifurcation of the middle omental artery near the lower end of the omentum. In type 2 the middle omental artery bifurcates midway between the gastroepiploic arcade and the lower end of the omentum. In type 3, it bifurcates 2-3 cm from the gastroepiploic arcade. In type 4 the middle omental artery is absent and the right and left omental arteries form the omental vascular arcade. In type 5, the terminal panch of the splenic artery develops into the left omental artery and the right gastroepiploic artery gives rise to the middle omental artery. The knowledge of these types of variations is important as the line of division of the vessels depends on this.

In an evaluation of 40 greater omentum specimens we studied the gastroepiploic vessels and the lymphatic system including the number of lymph nodes (in areas measuring 10x10 cm), in order to understand its use in microsurgical techniques. Half of them proceeded from fresh cadavers without

digestive or oncologic pathology and the other half from plastic surgery patients in which different reconstructive procedures were performed using the greater omentum flap.

Macroscopic data reveled that the mean diameter of the arteries of the right gastroepiploic arcade was 2.9+/-0.4 mm; the mean diameter of the veins of the right gastroepiploic arcade was 3+/-0.6 mm. At the left gastroepiploic arcade, the mean circumference of the arteries was 2.5+/-0.6 mm and the mean diameter of the veins was 2.8+/-1.0 mm.

When visual analysis of the greater omentum was done at the portions extracted portions measuring 10 x 10 cm, we found a mean of 1.5 lymph nodes. It was remarkable that when dissection of the vascular pedicle was done under the microscope, many lymphatic vessels were observed around the blood vessels. The diameter of these vessels was ranging from 0.4 to 0.7 mm.

In the microscopic study of D2-40 labeled sections, we counted the number of lymphatic vessels in 6 different fields at x500 magnification. The mean value of lymphatic vessels was 5.2+/-1.2.

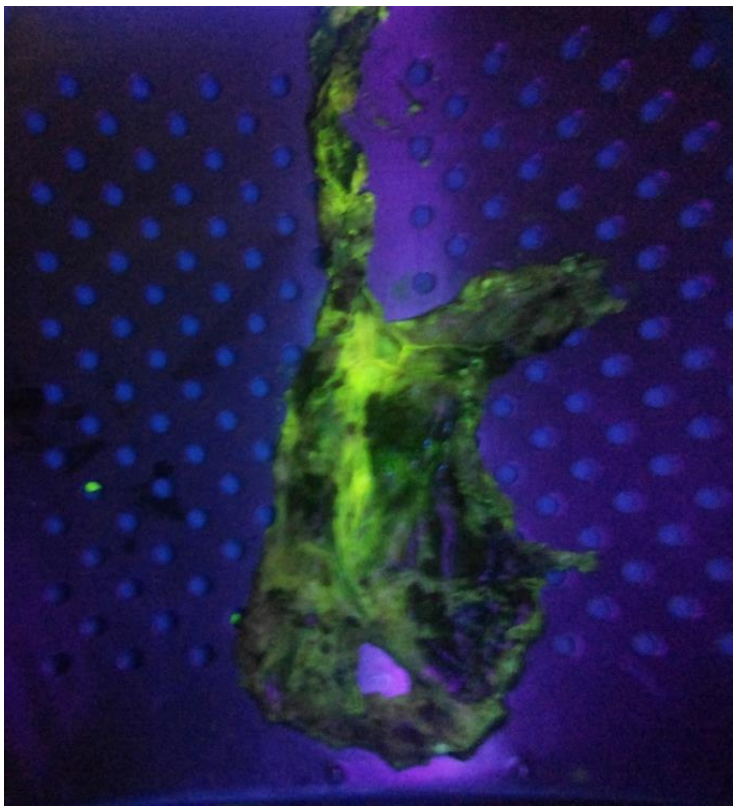

Figure 1a. Vascular arcade of the GO marked with fluorescein stain.

Figure 1b. A scissor is showing a lymphatic vessel marked with indocianine green.

Interestingly the omentum contains lymphoreticular bodies known as "milky spots" [27, 28] or omentum-associated lymphoid tissue. These "milky spots" were consequently described, presenting a diameter of less than 1.5 mm. We observed at least 2 spots in surfaces of 3 x 3 cm.

It is important to map and maintain these structures as the lymphatics of the omentum begin at the milky spots and drain into the lymphatic collecting system along the pedicle. The lymphatic capillaries in the milky spots initiate absorption from the peritoneal cavity [29]. Therefore, the omentum is potentially an ideal flap for draining lymphatic fluid. (Figure 1a and b).

THE ROLE OF THE GREATER OMENTUM IN RECONTRUCTIVE SURGERY AND IN LYMPHEDEMA SURGERY

Collecting the omentum for transposition or transfer as a reconstructive flap is well described in the surgical publications [30–32].

This is a highly vascularized protective intraabdominal structure that presents angiogenic properties that act as a natural defense mechanism in peritonitis and intra-abdominal sepsis [33].

The significance of the greater omentum has been discovered recently by surgeons of various disciplines because it provides an excellent plastic

material against inflammation, irradiation and for repair of defects that can be applied in the abdominal cavity; it can be exteriorized and lengthened at a vascular pedicle and detached using microvascular anastomoses [34].

It can be transferred to any site for reconstruction of radiation necrosis, pharyngostomy, thoracic empyema (especially those maintained by a bronchial fistula). In cancers of the oropharynx, the addition of a conjoint potion of the stomach allows reconstruction of gastrointestinal continuity. In traumatology, an omental free flap can save a leg or a foot, with bony disruption and major soft tissue destruction [35]. It has also been used to treat Fournier's gangrene as a free flap [36].

According to Hultman [37] the most common donor-site complications of omentoplasty included abdominal wall infection, fascial dehiscence and symptomatic hernia.

The use the greater omentum in the management of chronic lymphedema has been evaluated clinically in many series, presenting satisfactory results as a pedicled flap and also as a free flap [38-41]. Based on the angio- and lymphangio-architecture of the gastroepiploic architecture large segments of greater omentum as a free autotransplant with microrevascularization to the femoral or axillary artery and vein thereby avoiding technical drawbacks of a pedicle graft were used for lymphedema treatment. Elongation of the omentum must be done properly because omental lymphatic arcades do not consistently follow the blood vascular arcades in its more distal part.

Other authors stated that omentum shall be used to prevent lymphedema after ilioinguinal lymph node dissection [42], but results were not coincident with clinical trial published by Ngan [43].

SURGICAL CONSIDERATIONS ABOUT THE PEDICLED GREATER OMENTUM FLAP

Since in 2005 Benoit [42] suggested that pedicled omentoplasty could be considered as an effective therapy for lymphedema of the lower extremity, an evolution of the surgical technique has been developed. Despite the fact that the greater omentum has been overlooked for the treatment of lymphedema because of presumed high morbidity, including the need for celiotomy and pedicle complications, when a meticulous surgical technique is followed during dissection, complications shall be dramatically reduced.

Obviously, the role of the greater omentum as a pedicled flap for the treatment of lymphedema shall be focused in the lower limbs and also for the treatment of penis and scrotal lymphedema.

Harvesting the greater omentum must be done following a standard open laparotomy. This is not contraindicated in patients with previous abdominal surgeries, but caution must be taken in these cases, because intrabdominal adherences can be found and also partial atrophies of the greater omentum.

An upper midline lapartomy incision is used and the omentum is delivered into the operative field. The greater curvature of the stomach and the right and left gastroepiploic vessels are identified as are the major descending branches to the omentum. The omentum is flipped superiorly (Figure 2), exposing the posterior attachements to the large colon. These attachments are freed, with perforating vessels ligated and divided. The omentum is then isolated on its attachment to the greater curvature of the stomach.

The second step consists on selecting the main vascular pedicle that is going to mantain the perfusión of the flap. This is a type III flap, following the classification of Mathes and Nahai [30].

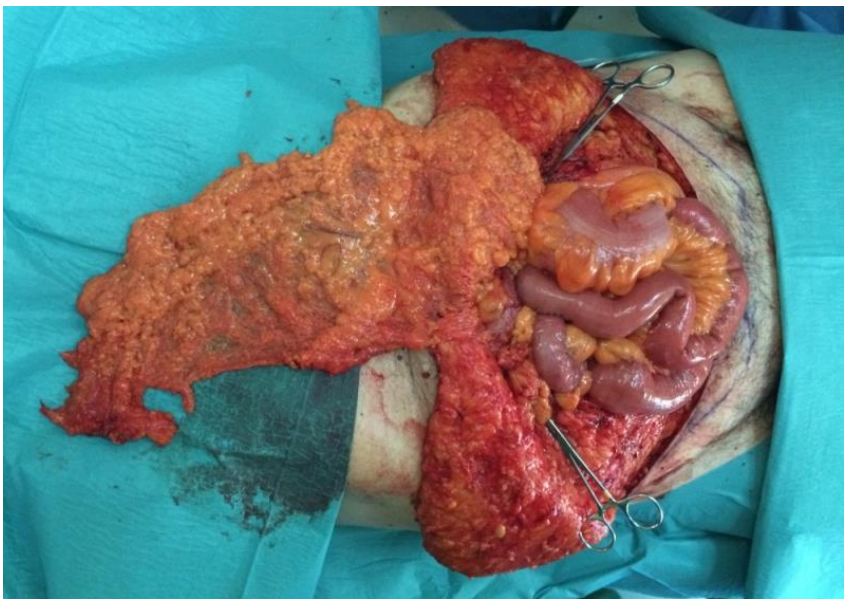

Figure 2. Exposure of the GO flap after laparotomy.

It presents two main pedicles: the right and left gastroepiploic vessels, being the right pedicle longer and wider than the left one. Nevertheless a surgical exploration will determine which pedicle will be elected when harvesting the flap. The election will also depend on the affected limb, being of preference the selection of the homolateral pedicle when there is not an

anatomical impairment. Nevertheless, before doing the ligation of the pedicle that is going to be sacrificed it shall be important to test the vascular flow in both arcades, using an intraoperative doppler probe.

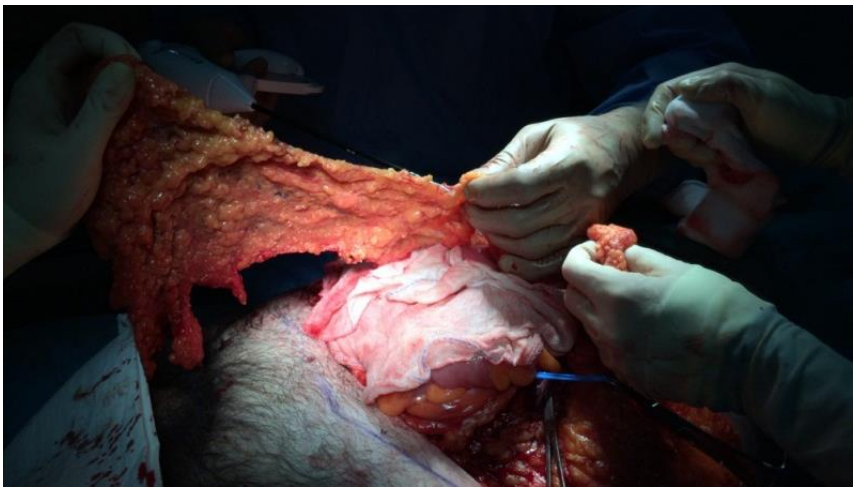

Figure 3a. Lengthening de GO flap. It is important to locate the vascular arcades by retroillumination.

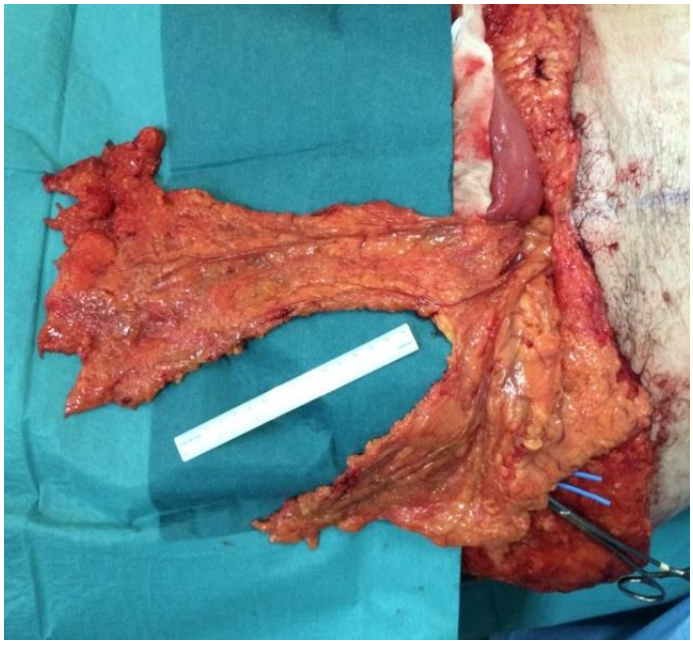

Figure 3b. It is possible to select a part of the flap and replace the rest; otherwise, we can divide it in 2 segments that may be placed in 2 different zones that need to be treated.

Once the selected pedicle is isolated, we proceed to elongate the flap (Figure 3a and b), to obtain the desired length to reach the groin or the

scrotum. A surgical exploration to evaluate that the perfusion is maintained at the distal end of the flap must be done.

Omental Lengthening

This was just described by Goldsmith and de Los Santos [44] for relief of chronic lymphoedema of the extremities in 1967. The omentum is freed from the transverse colon along the vascular plane and then from the greater curvature of the stomach taking care to preserve the gastroepiploic arcades and the blood vessels between the arcades. In doing so, the pedicle is based on either the right or the left gastroepiploic artery based on the dominance.

This pedicled graft is then lengthened depending upon the vascular anatomy and the panches along the greater curvature of the stomach are tied. The most frequently encountered complications include prolonged ileus and minor wound infection at the incision sites. Incisional hernia has been reported to occur from the abdominal incision site. Failures have been shown to result in patients in whom the mobilisation of the omentum has been improper. Majority of these complications occur if the surgeon is unfamiliar with the anatomy of the omental vascular arcade. Handling of the omentum should be gentle to prevent thrombosis of omental vessels and care should be taken to prevent omental torsion while tunnelling.

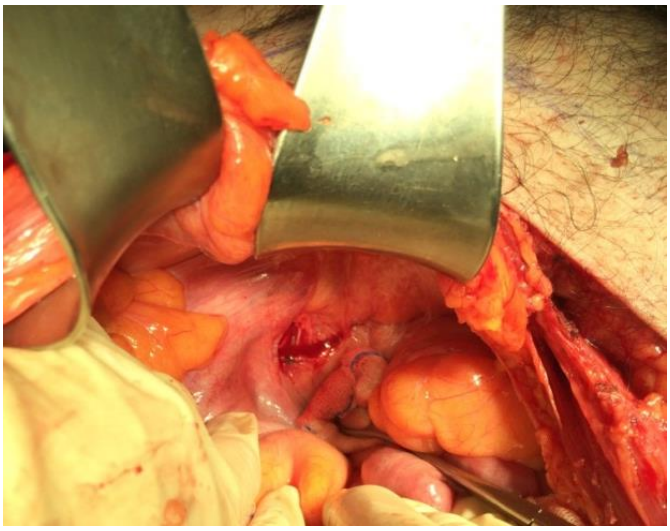

Figure 4. Exposure of the primitive iliac vessels.

It is of utmost importance to place the distal part of flaps into the desired anatomical area where the lymphatic drainage has been interrupted. When the

penis has to be treated, we prefer to place the flap around its base, in a subcutaneous layer. When there is a scrotal lymphedema, it is indicated to place the flap around the iliac vessels. In this case, we recommend to make a window in the peritoneus, in order to make a exposure of the iliac vessels (Figure 4). After dissection of the iliac vein, it should be wrapped with the flap (at least 2 cm in lenght).

This technique must be repeated at the femoral vein when the groin nodes must be replaced by the nodal groups of the flap. In these cases the flap shall be tunelized under the inguinal ligament but it could also be placed over this anatomical structure (Figure 5).

A subfascial tunnel is then prepared on the anteromedial aspect of the thigh and leg up to the ankle of the affected limbs after making multiple skin incision. The lengthened omentum is passed down through this tunnel from the abdomen and pelvis and even up to the ankle where it is anchored to the underlying muscle.

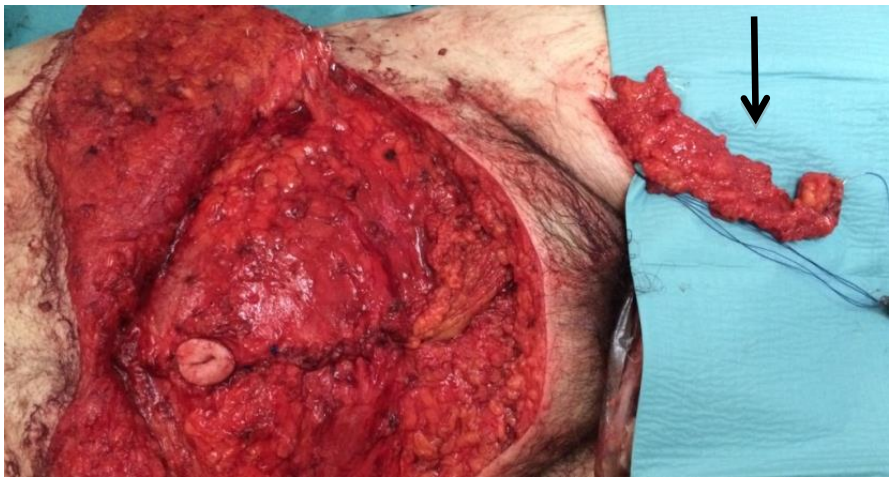

Figure 5. Tunelization of the GO flap to reach the groin región. The black arrow shows the distal part of the flap.

SURGICAL CONSIDERATIONS ABOUT THE FREE GREATER OMENTUM FLAP

It is known that advances in microsurgery have displayed promising results for the treatment of lymphedema and it has been remarked by some authors who recently published novel techniques and satisfactory results when using the free omental lymphatic flap for the management of lymphedema.

The minimally invasive harvest but also laparoscopic underminig of this flap successfully avoids both the associated morbidity when dissecting this flap and the risk of iatrogenic lymphedema to the donor site [8, 45].

MINIMALLY INVASIVE HARVEST OF THE GREATER OMENTUM FLAP

We recommend this approach specially for those cases in which simultaneous breast reconstruction is needed. If a DIEP flap or a TRAM flap is harvested, it is posible to perform a supraumbilical laparotomy at the midline of the abdomen, to make an exposure of the omentum, locate the gastroepiploic vessels and select the desired pedicle. At this point whe can obtain a half of the greater omentum and preserve the rest. It is important to dissect under magnification loupes the selected gastroepiploic artery and vein, in order to make the transection of them under control, using microsurgical instruments. The next clincal case will explain with detail how this technique should be done.

A 69-year-old woman underwent left breast cancer surgery 33 years ago. Halsted radical mastectomy, radiotherapy and chemotherapy were performed but information regarding type of chemotherapy drugs was unknown. Four years later, she presented with 4^{th} rib exposure due to osteoradionecrosis. She had also developed lymphedema of the left upper limb of unknown start date. Clinical rehabilitation was done irregularly. Associated medical history was idiopatic epilepsy, Parkinson's disease and depressive disorder. She was living in a residence for disabled patients.

Physical examination showed a narrow thorax with malposition of the left clavicle due to a severe fracture ten years previously. BMI was 25.24, height was 158cm and weight was 62.6kg.

A lymphedema of the left upper limb and the hand was observed with numbness and pitting edema. Preoperative circumference difference between the upper extremities was 87.5cm. Measures were taken at the palmar crease, at the wrist, 10, 20 and 30 cm proximal to it.

Lymphoscintigraphy showed a normal sequence at the right limb and dermal backflow at the left arm with no identification of lymph nodes.

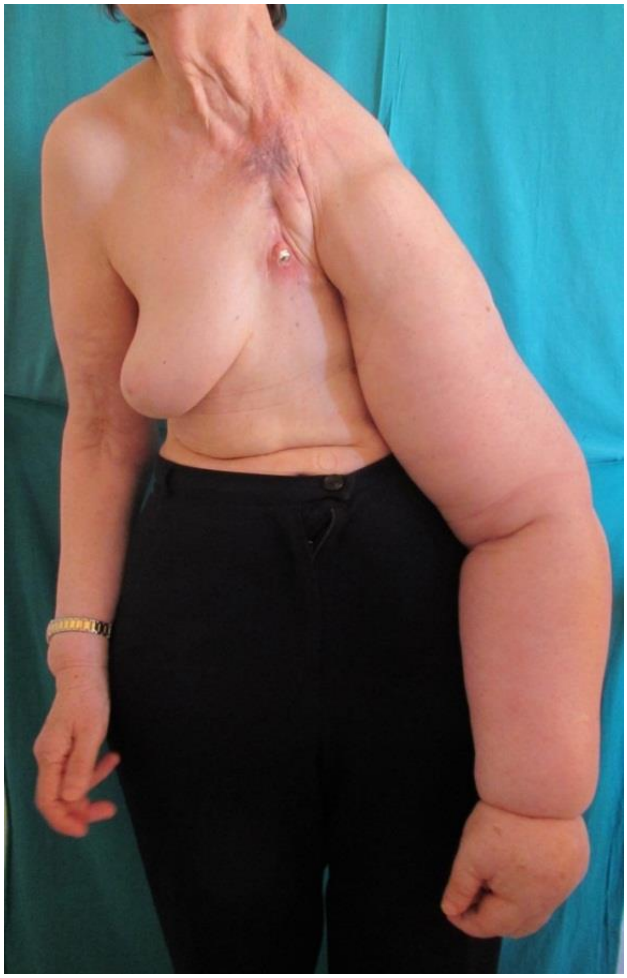

Figure 6. Severe cronic lymphedema affecting the left upper limb and radionecrosis at the chest wall, with exposition of a rib.

Diagnosis was stage III (ISL) lymphedema secondary to radical mastectomy and osteoradionecrosis of the 4th and 5th ribs with associated ulcer of the chestwall (Figure 6).

A TRAM flap, based on the contralateral muscle (right one) was harvested, after removal of anterior portion of both ribs. The deep epigastric vessels were dissected proximally to their origin in order to prepare a recipient vascular pedicle in which anastomoses of the gastroepiploic vessels could be done. When the TRAM flap was undermined, a partial supraumbilical laparotomy was done, and the greater omentum was exposed. It was adhered to the small one, due to previous abdominal surgery. Dissection of the greater omentum was done carefully and under the surgical microscope, the right gastroepiploic vessels were dissected.

Figure 7. End-to-end microvascular anastomosis of the pedicle of the GO flap to de deep inferior epigastric vessels.

Closure of the abdomen was done using a mesh. Anastomoses of the gastroepiploic vessels were done end to end to the deep inferior epigastric vessels and a portion of the omentum measuring 6 per 9 cm was placed under the superficial fascia of the inner aspect of the arm, from the axila, to the inner midline of the humerus (Figure 7).

After 24 months, the patient presented a significant improvement of the limb, in which we could appreciate an improvement of numbness at the hand, showing many wrinkles on the dorsum. The difference of the circumferences between both limbs is currently 68 cm (Figure 8).

Figure 8. Postoperative picture of the left upper limb after 12 months.

LAPAROSCOPIC HARVEST OF THE GREATER OMENTUM FLAP

The laparoscopic undermining of this flap successfully avoids both the associated morbidity when dissecting this flap and the risk of iatrogenic lymphedema to the donor site, but this technique, must be done by a laparoscopic surgeon with the association of the plastic surgeon. The plastic surgeon has to make the selection of the pedicle and shall supervise its dissection. These vessels must be dissected carefully and the plastic surgeon must decide the point of ligation since it is essential to ensure that the size and quality of the vessels is adequate for the microanastomoses. Again, a clinical case will explain the way to proceed.

A 45 year-old woman was sent to our hospital for evaluation of a lymphedema affecting the right lower limb. Erytematous lupus was diagnosed 30 years ago. Kidney transplantation after renal failure associated to lupus nefropathy was done 9 years ago. Lymphedema began one year after the kidney transplantation.

Clinical rehabilitation was done since the development of the lymphedema, by means of manual lymphatic drainage and bandages, which were not well tolerated nor improved the clinical situation. Thus she was recommended to wear compressive pants daily. BMI was 35.52, height 151 cm and weight 81 kg. A cronic lymphedema affecting the right lower limb and foot (III degree ISL) was diagnosed. Numbness of the skin with fovea was remarkable, without pain; the difference of diameters between both limbs was 83.7 cm. (Circumferences were measured at 5 different points along the limb).

Lymphogammagraphy showed a normal sequence at the left lower limb and dermic impregnation at the right leg without visual identification of lymph nodes. Initially lymphovenous anastomoses were recommended. This surgery failed but the patient demanded a new surgery for lymphedema.

This time, a free greater omentum flap transfer to the inguinal region was indicated. The patient was operated under general anesthesia.

GO was dissected by laparoscopy, taking special care in the dissection of the left gastroepiploic arteries and veins, in order to avoid any damage of it. Dissection of these vessels was advised by a plastic surgeon as we already described. The extraction of the surgical specimen out of the abdomen was done carefully, in order to avoid any lesion of the vascular pedicles (Figure 9). This point is essential, because torsion of the vessels or excessive compression or elongation can be devastating when doing the microsurgical timing.

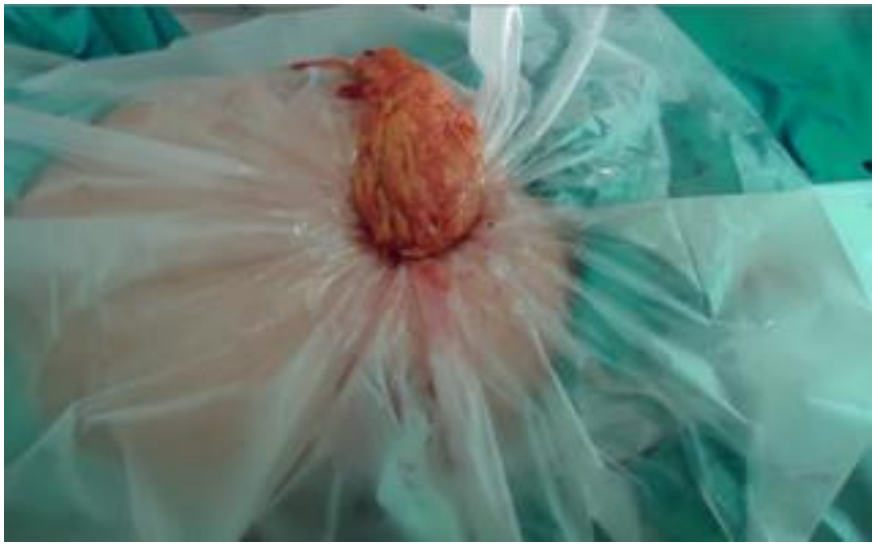

Figure 9. Extraction of the GO flap through a small incition at the abdominal wall after laparoscopic dissection.

Figure 10. After microanastomoses are performed at the groin area, we proceed to place the flap at the Scarpa's triangle.

The free flap vessels were anastomosed to the right superficial circumflex iliac (SCIEA) system. The venous anastomosis presented some problems due to the fragility of the wall of the right gastroepipoic vein, which required an arterial interposition graft proceeding from the distal part of the donor SCIEA.

The left gastroepiploic vessels were selected because this part of the omentum was preserved better than the right one (Figure 10).

Half of the greater omentum was placed subcutaneously, at the triangle of Scarpa, and its distal portion was exposed through a small tunnel to explore the viability of the flap at the postoperative period (Figure 11).

Figure 11. Viability of the distal part of the free GO flap.

Figure 12. Preoperative view after GO free flap transfer and postoperative view after 12 months.

The patient presented a good recovery and 12 months after surgery she referred a high degree of satisfaction, the leg being lighter, with a smaller circumference at different points. The difference of diameters was 69 cm one year after the surgery (Figure 12a and b).

POSTOPERATIVE CARE

After surgery patients must be under strict surveillance for flap monitoring and controlling gastrointestinal peristalsis.

We recommend the use of a Doppler probe to evaluate both arterial inflow and venous outflow of the vascular pedicle of the nodal GO flap. Another possibility for monitoring is to create a subcutaneous tunnel to expose the distal part of the flap. This technical detail allows an evaluation of the viability of the GO. If there is any doubt about it, it shall be possible to make it bleed with a gauze.

Enteral nutrition must be started when there is evidence of gastrointestinal motility. Otherwise we prefer to discharge patients 5 days after the surgery.

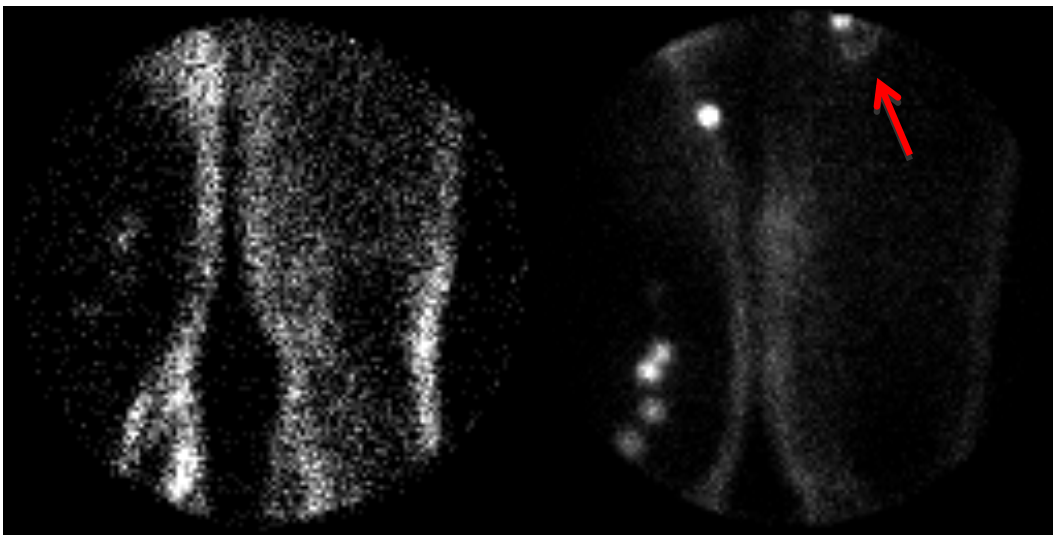

Figure 13. Preoperative and postoperative lymphographies. The one on the right shows a new image (red arrow), corresponding to a transplanted nodal group 12 months after the surgery.

Manual lymphatic drainage must be started 3 weeks after the surgery. Until this moment, the limb must wear non compressive garments. Once physiotherapists start lymphatic drainages, compression garments must be used during the next 3 months. Patients receive 2 sessions per week. After this

period, garments are changed to elastic bandages which are used permanently along the next 3 months. After 6 months from surgery patients are invited to remove the elastic bandages, in order to alter it with periods rest. Depending on the severity of the lymphedema, the time of evolution of the disease and the response to surgery, patients will be obliged to wear it for a longer period of time or not. Lymphography must be done 12 months after the surgery, but never before the 6^{th} month (Figure 13) after it, since the transferred nodal groups needs time to recover the activity.

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Chapter 3

MOLECULAR MECHANISMS OF TUMOR LYMPHANGIOGENESIS

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ABSTRACT

The lymphatic vascular system plays a major role in cancer metastasis. Metastasis of cancer cells to regional lymph nodes is the first step in tumor dissemination and is particularly important for cancer prognosis. The metastatic spread of tumor cells to lymph nodes is enhanced following the induction of tumor lymphangiogenesis. Therefore, the manipulation of lymphangiogenesis may provide a potential therapeutic benefit. The formation of a lymphatic vascular system is a dynamic process during embryogenesis. In embryos, the blood circulatory system is first to evolve, followed by specification of lymphatic endothelial progenitor cells differentiated from blood vascular endothelial cells and budding of these cells from the cardinal vein. Under normal physiological postnatal conditions, however, the formation of new lymphatic vessels scarcely occurs. In adults, lymphangiogenesis only takes place during certain pathological conditions such as inflammation, tissue repair, and tumor growth. Postnatal lymphatic vessel formations

have been assumed to occur mainly by hyperplasia of lymphatic vessels themselves, or sprouting from pre-existing lymphatics. The relative contribution to the formation of new vessels from circulating endothelial progenitor cells is not clearly understood. The recent identification of lymphatic endothelial specific markers, such as hyaluronic acid receptor-1 (LYVE-1) and podoplanin, has greatly increased attention on how lymphangiogenesis, the growth of lymphatic vessels, is regulated in the tumor microenvironment. Accumulating evidence suggests the involvement of bone marrow-derived lymphatic progenitor cells in tumor lymphangiogenesis. Studies over the past two decades have revealed the growth factors involved in lymphatic endothelial cell growth and migration. In this review, we summarize the recent development of the molecular mechanisms of tumor lymphangiogenesis, especially the role of bone marrow-derived cells and the growth factors implicated in this process.

INTRODUCTION

The metastatic spread of tumor cells to distant organ is the leading cause of mortality from cancer. Although metastatic tumor spread can occur via a variety of mechanisms including direct local invasion of tissue or the seeding of body cavities, most metastases arise following invasion of and dissemination via the circulatory systems. While both the blood and lymphatic vascular systems have played pivotal roles, preclinical experimental systems supported by clinical evidence suggest the most common pathway of initial metastasis is through the lymphatic system. In most of human cancers, the detection of tumor metastasis in the tumor-draining lymph node is the first step in tumor dissemination and is one of the most important markers for both patient prognosis and therapeutic strategy decisions. The elucidation of the lymphangiogenic mechanism is expected to lead to the establishment of new anti-cancer therapy.

The formation of a lymphatic vascular system is a dynamic process during embryogenesis. In embryos, the blood circulatory system is first to evolve, followed by specification of lymphatic endothelial progenitor cells differentiated from blood vascular endothelial cells and budding of these cells from the cardinal vein [1]. During embryogenesis the development of lymphatic system is controlled by the sequential activation of transcription factors, such as prosper-related homeodomain transcription factor (PROX1), Sox18, COUP-TFII and so on [2].

The members of the vascular endothelial growth factor (VEGF) family play major roles in lymphangiogenesis [3-5]. The proliferation and migration of lymphatic endothelial progenitor cells is mediated by VEGF receptor 2 (VEGFR2) and VEGFR3 signals, which are mainly driven by VEGF-C and VEGF-D [6]. Downstream of these receptor tyrosine kinases, protein kinases Akt and ERK1/ERK2 are activated [3, 4]. These signaling pathways are modulated by VEGFR3 co-receptor neuropilin 2 (NRP2) and collagen and calcium binding EGF domain-containing protein 1 (CCBE1) [2].

In order to analyze tumor lymphangiogenesis, the specific molecular markers which discriminate between blood and lymphatic vessels, are indispensable. Several proteins have been identified which are expressed in lymphatic endothelial cells, including PROX1, NRP2, VEGFR3, hyaluronic acid receptor-1 (LYVE-1), podoplanin and so on [3, 6, 7]. LYVE-1 is a CD44 homolog, which is involved in hyaluronic acid transport and is expressed in embryonic and adult lymphatic endothelial cells. Podoplanin is a mucin-type transmembrane glycoprotein expressed in lymphatic endothelial cells, which is required for lymphatic development. This glycoprotein is not expressed in blood vessels and is a useful marker of lymphatics. VEGFR3 is a receptor tyrosine kinase primarily involved in lymphangiogenesis. This receptor is predominantly expressed on lymphatic endothelial cells, but also on some fenestrated blood vessels and on some blood endothelial cells during tumor angiogenesis [8]. Therefore, it is not an adequate marker to study tumor lymphangiogenesis. In the recent years, LYVE-1 and podoplanin have been routinely used to study lymphangiogenesis and lymphatic vessel remodeling in cancer [4, 7, 9].

The growth of new lymphatic vessels, called lymphangiogenesis, is largely absent in adults, but can be induced in pathological processes, such as inflammation, wound healing and cancer [4, 10, 11]. Lymphatic vessels were used to be considered as passive participants in tumor metastasis by simply protruding channels for tumor cells to transit through. However, the utilization of key lymphatic-specific molecular markers, podoplanin and LYVE-1, and the recent elegant experimental systems in vivo and in vitro to study lymphatic biology have revealed a much more complex and rather an active role for the lymphatic vasculature in metastatic tumor spread [12]. The lymphatic system has evolved from a relatively passive model to an active system organized by a variety of lymphangiogenic growth factors, chemokines, and their receptors in cancer metastasis. In the majority of clinical studies, a significant correlation has been observed between lymphatic vessel density and lymph node and organ metastasis [13-17]. This has led to the concept that the denser the

lymphatic vasculature within or close to the tumor, the more potential entry sites the tumor cells have to vessels that could be used as highways for metastatic spread. Therefore, the blockade of tumor lymphangiogenesis by targeting lymphangiogenic signaling pathways could be a useful therapeutic strategy to prevent cancer metastasis.

MOLECULAR MECHANISM OF TUMOR LYMPHANGIOGENESIS

The formation of a lymphatic vascular system is a dynamic process during embryogenesis. Under normal physiological postnatal conditions, however, the formation of new lymphatic vessels scarcely occurs. In adults, lymphangiogenesis only takes place during certain pathological conditions such as inflammation, tissue repair, and tumor growth. Postnatal lymphatic vessel formations have been assumed to occur mainly by hyperplasia of lymphatic vessels themselves, or sprouting from pre-existing lymphatics [6].

Several factors with prolymphangiogenic activity have been identified to date. These include VEGF-A, VEGF-C, VEGF-D, FGF, and so on [3]. VEGF family was originally characterized as factors that promote either angiogenesis or lymphangiogenesis without major overlaps between the two processes. During subsequent studies, however, this view has become more complex as various forms of VEGF family and several co-receptors have been discovered. VEGF-C and VEGF-D were identified as the first lymphangiogenic factors that bind lymphatic endothelial VEGFR3 [6]. VEGF-C and VEGF-D also activate VEGFR2, which is initially identified as a potent mediator of angiogenic signaling [4, 5]. Activation of the latter receptor tyrosine kinase by VEGF-E, a viral-derived VEGF resulted in inducing angiogenesis but not lymphangiogenesis [18]. However, activation of VEGFR2 by VEGF-C or VEGF-A was also shown to promote lymphangiogenesis in tumor [19, 20]. ZM323881, a selective inhibitor of VEGFR2 decreased of proliferation and migration of lymphatic endothelial cells [21]. The expression levels of VEGFR2 on lymphatic endothelial cells and the response to VEGF-C or VEGF-A seem to vary depending on the tissue microenvironment.

Table 1. Murine xenograft model experiments of tumor lymphangiogenesis

Origin of cancer cells	Cell line	Axis of lymphangiogenesis	Experimental approach	Reference
Lung cancer	Murine Lewis lung cancer cell line	VEGF family/VEGFR3	Murine model of subcutaneous implantation of mixed cancer and bone marrow cell	[21]
		VEGF-C/VEGFR3	GFP-BM transplantation murine model of subcutaneous implantation of cancer or/and VEGF-C	[22]
	Human A549 lung cancer cell line	Positive cofactor 4 (PC4)/VEGF-C,-D/VEGFR3	Murine model of subcutaneous implantation of cancer	[16]
Gastric cancer	Human SGC-7901 gastric cancer cell line	VEGF-C	Murine model of subcutaneous implantation of cancer, and oral administration of drug	[23]
	Human MKN45 gastric cancer cell line	VEGF-A	GFP-BM transplantation murine model of subcutaneous or stomach implantation of cancer	[24]
Colorectal cancer	Human HT-29 colon cancer cell line	VEGF-A,-C,-D/VEGFR2,3	Murine model of intraperitoneal implantation of cancer	[25]
	Human LS174T colorectal cancer cell line	VEGF-A	GFP-BM transplantation murine model of subcutaneous implantation of cancer	[26]
Breast cancer	Human SK-BR-3 breast cancer cell line	VEGF-A	GFP-BM transplantation murine model of subcutaneous implantation of cancer	

Table 1. (Continued)

Origin of cancer cells	Cell line	Axis of lymphangiogenesis	Experimental approach	Reference
Breast cancer	Murine 4T1, Cl66 and Cl66M2 breast cancer cell line	VEGF-C/VEGFR3	Murine model of breast implantation of cancer, and intraperitoneal administration of MAZ51	[27]
	Human MDA-MB-231 breast cancer cell line	CCL21 chemokine/CCR7 chemokine receptor/VEGF-C	Murine model of subcutaneous implantation of cancer	[28]
		VEGF-C/superoxide dismutase 3 (Sod3)	Murine model of breast implantation of VEGF-C knockdown cancer	[29]
		IGF1/IGF1R and HGF/Met	Murine model of intraperitoneal implantation of cancer and SP2043	[30]
Hepatic cancer	Human HepG2, HuH7 and Hep3B hepatocellular carcinoma cell line	VEGF-D/VEGFR3	Murine model of subcutaneous and liver implantation of cancer	[13]
Pancreatic tumor	Rip1Tag (Insulinoma murine model)	VEGF-C,-D/VEGFR3	GFP-BM transplantation murine model of subcutaneous implantation of cancer	[31]
Prostatic cancer	Murine TRAMP-C1 prostatic cancer cell line	VEGF-C,-D/VEGFR3	GFP-BM transplantation murine model of subcutaneous implantation of cancer	
	Human LAPC-4, LAPC-9, CWR22Rv-1, and PC3 prostatic cancer cell line	VEGF-C/VEGFR3	Murine model of subcutaneous implantation of cancer	[32]

Origin of cancer cells	Cell line	Axis of lymphangiogenesis	Experimental approach	Reference
Skin cancer	Murine model of chemically induced skin carcinogenesis	VEGF-C/VEGFR3	VEGF-C overexpression transgenic murine model of chemically induced skin carcinogenesis	[14]
		VEGF-A/VEGFR2	GFP in epidermal keratinocytes transgenic murine model or VEGF-A overexpression transgenic murine model of chemically induced skin carcinogenesis	[20]
	Murine B16-F1 melanoma cell line	VEGF-C/VEGFR3	GFP-BM transplantation murine model of subcutaneous implantation of cancer or/and VEGF-C	[22]
Fibrosarcoma	Murine T241 fibrosarcoma cell line	VEGF family/VEGF2,3	GFP-BM transplantation murine model of subcutaneous implantation of cancer	[19]

Table 2. Tumor lymphangiogenesis examined in human surgical specimens

Origin	Axis of lymphangiogenesis	Reference
Non-small-cell lung cancer	(VEGF-C)/VEGFR3	[15]
Gastric cancer	Akt+mTOR/VEGF-C,-D	[33]
	-	[17]
		[34]
		[35]
Esophageal squamous cell cancer	VEGF-C/VEGFR3	[36]
Urothelial cancer of bladder	VEGF family	[37]

For tumor lymphangiogenesis, attention has been focused on the role of VEGF-C and VEDF-D, and their receptors VEGFR2 and VEGFR3 in recent years both in murine tumor xenograft experiments (Table 1) and human surgical specimens (Table 2). High expression levels of the lymphangiogenic factor VEGF-C in patient samples correlate with lymph node metastasis in a number of tumor types. Using murine models, overexpression of VEGF-C or VEGF-D has been shown to increase lymphatic vessel density, vessel diameter and lymph node and organ metastasis of many cancer types [13, 14, 20, 22, 29]. The effects of VEGF-C have been described in detail in lung cancer and melanoma models [22]. VEGF-C caused dilation of peritumoral lymphatic vessels and sprouting of new lymphatic vessels to closely surround the malignant cells. VEGF-C-induced dilation of collecting vessels around tumors may allow the entry of clusters of metastatic tumor cells. The role of VEGF-C/VEGFR3 is also confirmed in the murine experimental models with several types of cancers, including breast cancer [27], pancreatic cancer [31], prostatic cancer [31, 32] and melanoma [22]. Even tumors that rarely metastasize through the lymphatic vessels have been observed to do so when manipulated to overexpress VEGF-C [38, 39]. VEGF-D overexpression in murine models with human hepatic cancer cells resulted in increased lymphangiogenesis and metastasis [13]. However, the correlation between VEGF-D expression levels and lymph node metastasis in patient samples has been found only in less than half of the studies. VEGF-D may play a limited role in tumor lymphangiogenesis, as low expression levels have been found in several patient-derived cell lines [7, 8, 26].

The various agents, which interfere with VEGF-C/-D and VEGFR2/3-dependent tumor lymphangio-genesis reveal the molecules modulating these signaling systems. These include VEGFR3 co-receptor NRP2 [40], WNT1, cyclooxygenase 2 [23], and so on [4, 6]. In addition to VEGF-C/-D and VEGFR2/3, they are potential targets for anti-lymphangiogenic therapeutic strategy.

Despite its initial recognition as a master regulatory molecule in angiogenesis [41, 42], the recent studies indicate that VEGF-A also plays a role in lymphangiogenesis in tumor [43, 44] as well as inflammation [45, 46] and wound healing [47] models. A role for VEGF-A in tumor-mediated lymphangiogenesis and lymph node metastasis has also been reported in murine fibrosarcoma xenograft models [48]. Transgenic mice that overexpressed VEGF-A in skin were susceptible to skin carcinogenesis in response to chemical inducers [20]. In our studies, three malignant adenocarcinomas, human gastric cancer MKN45 cells, human colorectal

cancer LS174T and human breast cancer SK-BR-3 cells, which produced tumor mass and promoted tumor lymphangiogenesis in murine xenograft models, predominantly secreted VEGF-A with minimal productions of VEGF-C and VEGF-D [26]. Our results also suggest the possible involvement of VEGF-A in the recruitment of lymphangiogenic epithelial progenitor cells from bone marrow in tumor lymphangiogenesis [26]. The same possibility is also shown in murine experimental models with Lewis lung cancer cells [21]. Overexpression of VEGF-A resulted in the formation of intratumoral lymphatic vessels and enlargement of peritumoral lymphatic vessels in squamous cell carcinomas [14, 20]. Various types of human cancer cells extensively secrete VEGF-A and this ability is often associated with poor prognosis [41, 42, 49, 50]. VEGF-A is a key factor of new blood vessel formation "angiogenesis" to support tumor growth and metastatic dissemination [41, 42]. VEGF-A may indirectly induce lymphangiogenesis via recruitment of VEGF-C/-D producing macrophages [11]. The role of VEGF-A seems to vary depending on the tissue microenvironment [20, 44, 46, 47]. Moreover, recent reports have demonstrated the immunosuppressive effects of VEGF-A by induction of regulatory T cells [50, 51] and by reduction of cytotoxic T cell activity [52]. These results suggest that VEGF-A could be a potential target for anti-lymphangiogenic therapy in addition to anti-angiogenic strategy [4, 7].

POTENTIAL ORIGINS OF TUMOR LYMPHATIC ENDOTHELIAL CELLS

For tumor angiogenesis, potential cellular origins of blood vascular endothelial cells include the pre-existing vasculature, circulating endothelial precursors and tumor cells [49]. Tumor blood vessels primarily develop by sprouting or intussusception from pre-existing vessels. Circulating endothelial progenitor cells from bone marrow also contribute to tumor angiogenesis. Tumor cells, which grow around existing vessels, also play a role to form a perivascular cuff.

Postnatal lymphatic vessel formations have previously been assumed to occur mainly by hyperplasia of lymphatic vessels themselves, or sprouting from pre-existing lymphatics [1]. A considerable number of studies initially demonstrates that the newly formed lymphatic vessels around tumor arise from the pre-existing lymphatic vasculature. However, the recent reports suggest

that the potential origins of lymphatic endothelial cells include trans-differentiation from other types of cells including bone marrow-derived lymphatic endothelial progenitor cells, bone marrow derived mesenchymal stem cells, bone marrow-derived macrophages, blood endothelial cells and cancer stem cells in addition to the pre-existing local peripheral lymphatic endothelial cells (Table 3). Possible involvement of blood endothelial cells and cancer stem cells awaits for further reevaluation, because in these reports [55-58] lymphatic vessels were recognized by an antibody against VEGFR3, which was also expressed on some fenestrated blood vessels and on some blood endothelial cells during tumor angiogenesis [8]. It has long been debated whether cancer stem cells play an active role in tumor lymphangiogenesis. The role of the tumor microenvironment also has been emphasized by description of tumor-associated macrophages that may function as a second source of lymphangiogenic factors [54].

Table 3. Possible origin of tumor lymphatic endothelial cells

Origin of cells	Cancer cells / specimens	Reference
Peripheral lymphatic endothelial cells	Murine Lewis lung cancer cell line Murine B16-F1 melanoma cell line	[22]
Bone marrow-derived lymphatic endothelial progenitor cells	Human MKN45 gastric cancer cell line Human LS174T colorectal cancer cell line Human SK-BR-3 breast cancer cell line Rip1Tag2(murine model of insulinoma) Murine TRAMP-C1 prostatic cancer cell line Murine T241 fibrosarcoma cell line	[19, 24, 26, 31]
Bone marrow-derived mesenchymal stem cells	Human DLD-1 colon cancer cell line	[5, 53]
Bone marrow-derived macrophages	Murine B16-F1 melanoma cell lne	[54]
Blood endothelial cells	Human breast cancer specimens	[55]
Cancer stem cells	Human glioblastoma specimens Human breast cancer specimens	[56-58]

The recent studies reveal the contribution of lymphatic endothelial progenitor cells for tumor lymphangiogenesis (Table 4). The role of circulating endothelial progenitor cells from bone marrow was first evaluated by an elegant murine tumor xenograft models with chimeric mice bearing green fluorescent protein (GFP)-positive bone marrow [22]. In these models, murine Lewis lung carcinoma or B16-F1 melanoma cells formed tumor masses and promoted tumor lymphangiogenesis, which led to dissemination of cancer cells via the lymphatic systems. However, the integration of bone marrow-derived cells with GFP fluorescence into tumor lymphatics verified with a lymphatic-specific marker LYVE-1 was not detected. Therefore, the involvement of bone marrow cells in tumor lymphangiogenesis was initially denied.

Table 4. Participation of bone marrow-derived progenitor cells in tumor lymphangiogenesis assessed by murine tumor xenograft models

Cell line	Conclusion	Reference
Murine Lewis lung cancer cell line	Bone marrow-derived mesenchymal stem cells drive peritumoral lymphangiogenesis via production of VEGF-A. (But they are not incorporated into peritumoral lymphatics.)	[21]
Human MKN45 gastric cancer cell line	Cancer cells represented recruitment and incorporation of bone marrow-derived lymphatic endothelial progenitor cells into gastric lymphatics.	[24]
Human LS174T colorectal cancer cell line, Human SK-BR-3 breast cancer cell line	VEGF-A produced by cancer cells induced the differentiation of bone marrow mononuclear cells into lymphatic endothelial lineage cells.	[26]
Rip1Tag (insulinoma murine model), Murine TRAMP-C1 prostatic cancer cell line	Cancer cells promoted the recruitment and incorporation of bone marrow-derived lymphatic endothelial progenitor cells into cancer lymphatics.	[31]
Murine T241 fibrosarcoma cell line	Bone marrow-derived cells were incorporated into normal and cancer lymphatics.	[19]

We have tested the possible involvement of marrow-derived progenitor cells in tumor lymphangiogenesis in the nude murine xenograft experimental models with human cancer cells [24, 26]. MKN45 gastric cancer cells were implanted under the gastric submucosa of GFP-positive bone marrow chimeric nude mice. After three weeks, LYVE-1-positive tumor lymphatics were detected around submucosa tumor mass. Nearly 50% of LYVE-1-positive tumor lymphatic cells also expressed GFP [24]. In the same experimental models of GFP-positive bone marrow chimeric nude mice, we have confirmed that human colorectal cancer LS174T cells and human breast cancer SK-BR-3 cells also recruited bone marrow-derived cells in the formation of tumor lymphatics [26]. These results indicate that bone marrow-derived lymphatic endothelial progenitor cells take a part in the human adenocarcinoma-induced lymphangiogenesis in addition to pre-existing lymphatics. Maertens L, et al. [21] also reported the involvement of bone marrow-derived cells in tumor lymphangiogenesis. Other reports showing the involvement of bone marrow-derived cells in tumor lymphangiogenesis is listed in Table 4 [19, 31]. The experimental data obtained to date collectively suggest that the newly formed lymphatic vessels around tumor arise from the pre-existing lymphatic vasculature and also from bone marrow-derived lymphatic endothelial progenitor cells.

In our studies, three human adenocarcinomas, gastric cancer MKN45 cells, colorectal cancer LS174T and human breast cancer SK-BR-3 cells predominantly secreted VEGF-A with minimal productions of VEGF-C and VEGF-D [26]. In the presence of VEGF-A, mouse bone marrow mononuclear cells became to express a lymphatic endothelial-specific marker, LYVE-1, in *in vitro* culture, as assessed by immunostaining as well as real-time PCR. These results indicate that VEGF-A is able to directly promote differentiation of bone marrow mononuclear cells into lymphatic endothelial lineage cells. VEGF-A-dependent recruitment of bone marrow-derived stem cells via VEGFR2 is also reported [21, 59]. Furthermore, VEGF-A may also indirectly induce lymphangiogenesis via recruitment of VEGF-C/-D producing macrophages [16]. However, mice with VEGF-C overexpression showed no integration of bone marrow-derived cells into newly formed lymphatics around the tumor [22]. These results suggest the possibility that VEGF-C/VEGFR3 takes a pivotal part in the survival, proliferation and migration of lymphatic lineage cells, and that VEGF-A plays an initial role in the recruitment of bone marrow progenitor cells and their differentiation to lymphatic lineage cells. Although the role of VEGF-A seems to vary depending on the tissue microenvironment [3, 17, 20, 25, 44, 46, 47, 60], this

growth factor thus is deeply involved in tumor lymphangiogenesis in addition to the well-characterized factors, VEGF-C and VEGF-D.

Table 5. Potential inhibitory approaches for tumor lymphangiogenesis

Types	Target	Drugs	Reference
Soluble receptor	VEGF-A	sVEGFR1	[21]
	VEGF-A,-C,-D	sVEGFR2	[21, 63]
	VEGF-C,-D	sVEGFR3	[13, 64-67]
Monoclonal antibody	VEGF-A	Bevacizumab	[61, 62]
	VEGF-C	VGX-100	[68]
	VEGF-D	VD1 cVE199	[69, 70] [71]
	VEGFR2	IMC-1121B(Ramucirumab), CDP791	[72]
	VEGFR3	hF4-3C5	[73]
Protein kinase inhibitor	VEGFR2	ZM323881 XL184(Cabozantinib)	[21] [74]
	VEGFR3	MAZ51 Sorafenib Pazopanib Sunitinib Axitinib Regorafenib	[4, 6, 27] [75] [76] [77, 78] [79] [80]
Others		siRNA PC4 Celecoxib Norcantharidin SP2043 LY294002, Rapamycin Saussureae radix, Psoraleae semen, Aurantti fructus immaturus	[16] [23] [25] [30] [33] [81]

POTENTIAL THERAPEUTIC APPROACHES

In order to prevent the progression of cancer, lymphangiogenic growth factors VEGF-C and VEGF-D, and their receptors VEGFR2 and VEGFR3 could be variable targeting candidates. Although VEGF-A was first identified as an angiogenic factor, this growth factor may also lead the activation of lymphangiogenesis [20, 21, 24, 26, 59]. The first target of an anti-angiogenic therapy was the ligand of VEGF-A. Bevacizumab, the VEGF-A blocking antibody is now clinically used for selective cancers in combination with chemotherapy. This strategy could also be useful to inhibit tumor lymphangiogenesis [61, 62].

Table 6. Successful inhibitory approaches for tumor lymphangiogenesis or lymphatic metastasis in murine tumor xenograft models or differentiation to lymphatic endothelial cells in culture

Inhibitor of lymphangiogenesis or lymphatic metastasis	Cell line	Reference
Animal experiments		
soluble VEGFR3	Human HepG2, HuH7, Hep3B hepatocellular carcinoma cell line	[13]
siRNA positive cofactor 4	Human A549 lung cancer cell line	[16]
soluble VEGFR1/2, and specific VEGFR-2 inhibitor (ZM323881)	Murine Lewis lung cancer cell line	[21]
COX-2 inhibitor (Celecoxib)	Human SGC-7901 gastric cancer cell line	[23]
Norcantharidin (+ mF4-31C1 or + Sorafenib)	Human HT-29 colon cancer cell line	[25]
VEGFR3 tyrosine kinase inhibitor (MAZ51)	Murine 4T1, Cl66 and Cl66M2 breast cancer cell line	[27]
Collagen IV biomimetic peptide SP2043	Human MDA-MB-231 breast cancer cell line	[30]
Culture experiments		
p-Akt inhibitor (LY294002) and p-mTOR inhibitor (Rapamycin)	Human SGC-7901 gastric cancer cell line	[33]
Saussureae radix, Psoraleae semen, Aurantti fructus immaturus	Murine Lewis lung cancer cell line Human Hela uterine cervical cancer cell line	[81]

To date, several new approaches have been developed to inhibit lymphangiogenic signaling pathways. These include soluble VEGF receptors to capture active VEGFs, neutralizing antibodies against VEGFs and VEGFRs, and chemical inhibitors interfering with VEGF signaling pathway (Table 5) [4, 7, 9]. The effects were first investigated in culture or murine tumor xenograft models, considerable numbers of studies showed that blockade of VEGF/VEGFR signaling restricts tumor lymphangiogenesis, enlargement of lymphatic vessels and lymph node metastasis (Table 6). For example, inhibition of the VEGF-C and VEGF-D receptor VEGFR3, either by a soluble receptor or by blocking antibodies acting as a ligand trap, has been shown to inhibit lymphangiogenesis [13, 64-67, 73], and to a moderate degree angiogenesis, and is also found to restrict lymph node metastasis without effects on mature vessels in surrounding tissues. Antibodies and soluble receptors are proteins and almost should be administrated to the patients intravenously. Small chemicals have also been developed, which can be orally administrated, although they have dose-limiting toxicities. Some of the anti-lymphangiogenic strategies are now in the preclinical or clinical trial stages [4, 7].

CONCLUSION

The metastasis of tumor cells is a leading cause of mortality in cancer patients. Metastasis of cancer cells to regional lymph nodes is the first step in tumor dissemination and is particularly important for cancer prognosis. The metastatic spread of tumor cells to lymph nodes is enhanced following the induction of tumor lymphangiogenesis. Knowledge of molecular mechanisms controlling lymphangiogenesis has significantly grown after the discovery of the responsible growth factors and receptors over the past two decades. Accumulating evidence facilitates the development of new therapeutic approaches targeting lymphatic vessels in cancer. Some of them are now in the preclinical or clinical trial stages and await further clinical validation. The VEGF-A blocking antibody “Bevacizumab” and the VEGFR2 blocking antibody “Ramucirumab” [72, 82], possible agents for not only tumor anti-angiogenesis but also tumor anti-lymphangiogenesis, are now clinically used for advanced cancer patients. We hope that similar new agent(s) will soon be in our hand in the near future.

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Chapter 4

NEW ROLES OF LYMPHANGIOGENESIS IN CANCER SPREAD

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ABSTRACT

The process of the formation of new lymphatic vessels from pre-existing vessels is called lymphangiogenesis.

Lymphangiogenesis plays a key role in the development and growth of tumors and their spread to other tissues.

Multiple molecular interactions between tumor cells and lymphatic endothelial cells initiate and maintain lymphangiogenesis.

The bond between vascular endothelial growth factor C (VEGF-C) and the tyrosine-kinase receptor VEGFR3 on lymphatic endothelial cells is the trigger signal that activates lymphangiogenesis.

Numerous research studies have assessed the relationship between VEGF-C and VEGF-D and tumor lymphangiogenesis. The aim of this chapter is to review molecular mechanisms related to the activation of tumor lymphangiogenesis and their clinical implications.

INTRODUCTION

Under normal physiological conditions, the cells of different tissues need oxygen and nutrients to survive. The blood vascular system facilitates the arrival of these nutrients and oxygen, whereas the lymphatic vascular system transports dietary fats from the intestine to the liver, contributes to the reabsorption of interstitial fluid (the lymphatic system collects about 10% of interstitial fluid), and collects waste products from tissue catabolism. The lymphoid organs of the lymphatic system also generate immune cells, which are part of the immune response to antigens.

In the absence of their own vascular system, the cells of a solid tumor subsist on diffusion mechanisms. These mechanisms allow the survival of tumor cells but prevent tumors from growing beyond 1 to 2 mm in size (Folkman 1990, 4). Tumors therefore need to create their own blood vessel network to grow. This vascular network enables the delivery of oxygen, nutrients, and growth factors. Tumor angiogenesis creates a blood vascular network connecting tumor tissue to systemic blood circulation.

Since Folkman began his work in the late twentieth century, tumor growth and metastatic tumor spread has been mainly associated with tumor angiogenesis. Until recently, lymph vessels were thought to play a passive role in lymphatic tumor spread. Lymphatic vessels have been described as structures through which circulating tumor cells reach lymph nodes in different territories. Currently, however, the lymphatic system is known to play an active role in the process of metastatic spread.

Induced tumor lymphangiogenesis (the formation of new lymphatic vessels from pre-existing lymphatics) establishes a lymphatic network that connects the tumor to the general lymphatic system. Moreover, these new intratumoral and peritumoral lymphatics allow the exchange of fluids and molecules between tumor cells and interstitial space. Furthermore, tumor lymphangiogenesis facilitates the arrival of tumor cells to the lymphatic system. From the lymphatic system, tumor cells can achieve blood circulation through the subclavian veins.

Tumor angiogenesis and tumor lymphangiogenesis are not independent processes. Both occur simultaneously and in a coordinated way, with the same molecular regulation as vascular endothelial growth factors and their receptors. In conclusion, the formation of a network of tumor-associated vessels allows tumor growth and metastatic spread. Therefore, it is crucial that we find new therapeutic agents to control angiogenesis and lymphangiogenesis to prevent

the growth and development of tumor metastasis (the major cause of death in cancer patients).

VASCULAR ENDOTHELIAL GROWTH FACTORS

Vascular endothelial growth factors (VEGFs) activate receptors on lymphatic endothelial cells acting at different cancer sites. VEGFs promote lymphatic remodeling and modulation of immune functions, thereby facilitating the spread of tumor cells to the lymph nodes. Tumor cells and stromal cells of tumors (tumor-infiltrating inflammatory cells and tumor-associated fibroblasts) produce vascular endothelial growth factors. Production of tumor vascular endothelial growth factors could be measured in circulating blood as an expression of these factors in tumor tissue.

The hypoxic tumor environment upregulates VEGF-C and VEGF-D and their expression in tumor tissue. The relationship between the overexpression of VEGF-C and VEGF-D and tumor lymphatic dissemination is also described herein.

VEGFs could circulate through the bloodstream or be transported inside platelets. Circulating levels of VEGF-C and VEGF-D can be determined in serum and plasma samples. As a significant portion of these factors are transported by platelets, complete levels can only be measured in serum samples. Serum levels are better for measuring circulating amounts of VEGF-C and VEGF-D.

The binding of VEGF-C and VEGF-D with VEGFR3 (tyrosine kinase receptors) is the main trigger signal to activate lymphangiogenesis.

Neuropilin 2 (NP2) acts as a coreceptor, modulating the signaling pathway activated by VEGF-C and VEGF-D.

VEGF or VEGF-A binds to the VEGFR1 receptor, activating angiogenesis. However, VEGF-A also promotes lymphangiogenesis by binding to the VEGFR2 receptor (Hirakawa 2005, 1090).

Numerous signaling pathways modulate lymphangiogenesis. Cyclooxygenase 2 (COX 2) is an enzyme that regulates prostaglandin synthesis and can promote lymphangiogenesis by regulating the expression of VEGF-C in tumors. The activation of endothelial nitric oxide synthase (eNOS) in lymphatic endothelial cells modulates tumor lymphangiogenesis. Other factors that can stimulate lymphangiogenesis are growth hepatocyte factor (HGF), angiopoetins 1 and 2 (Ang-1, -2), fibroblast growth factor-2 (FGF-2),

platelet-derived growth factor B (PDGF-B), eritropoietin, adrenomedullin, and epidermal growth factor (EGF) (Stacker 2014, 161–162).

A high density of lymphatic vessels in tumor tissue, high levels of circulating VEGFs, and overexpression of VEGFs in tumor tissue are related to lymphatic metastasis, distant metastasis, and worse prognoses (Stacker 2014, 167).

STRUCTURE OF THE LYMPHATIC VASCULAR SYSTEM

The lymphatic system consists of tissues and organs connected by lymphatic vessels. The lymphatic organs produce immune cells (leukocytes), which circulate with lymph through the lymphatic vessels. The initial lymphatic or lymphatic capillaries drain lymph toward larger vessels called collecting lymphatics. Lymphatic capillaries are formed by endothelial cells (without basement membranes). Collecting lymphatics have valves and smooth muscle cells, and collecting lymphatic vessels drain into the lymph nodes. The lymphatic vessels that drain toward the lymph nodes are called afferent lymph vessels, whereas the lymph filters through lymph node tissue and is collected by efferent lymph vessels. Efferent lymph vessels drain into another lymph node or may empty directly to the lymph ducts. The lymph ducts return lymph to the bloodstream by emptying into the subclavian veins (Albrecht 2013, 483–484).

TUMOR LYMPHANGIOGENESIS: THE FORMATION OF NEW LYMPHATIC VESSELS

The discovery of the molecular markers of lymphatic endothelial cells has allowed a breakthrough in the study of lymphangiogenesis. The main molecular markers often expressing lymphatic endothelial cells are LYVE1 (lymphatic vessel endothelial hyaluronan receptor), podoplanin (a type-1 transmembrane glycoprotein), the transcription factor PROX1, VEGFs and VEGFR3 (Albrecht 2013, 484).

During lymphangiogenesis, new lymph vessels are formed by lymphatic endothelial cells from pre-existing lymph vessels as well as endothelial cells originated by mechanisms of transdifferentiation from blood endothelial cells,

tumor-associated macrophages, bone marrow–derived mesenchymal stem cells, and even tumor stem cells (Li 2015, 444).

Lymphangiogenesis creates new intratumoral and peritumoral lymphatic vessels. The functional capacity of intratumoral lymphatic vessels appears to be limited, since most of these lymphatic vessels collapse because of chaotic tumor growth (Albrecht 2013, 488). Lymphangiogenesis in lymph nodes is a normal component of the immune response of the host (Podgrabinska 2014, 47). During tumor lymphangiogenesis, lymphatic vessels proliferate both in the sentinel node and in the more distal draining lymph nodes (Kerjaschki 2011, 2000–2001). Lymphangiogenesis in lymph nodes is referred to as lymphovascular niche. The appearance of these tumor niches promotes tumor metastasis.

TUMOR LYMPHANGIOGENESIS: LYMPHATIC ENLARGEMENT

There are changes in the structure of lymphatic vessels during lymphangiogenesis. These structural changes include lymphatic enlargement, which begins at peritumoral lymphatic capillaries. Lymphatic enlargement also affects most distal lymph vessels, such as collecting lymphatics in tumor-draining lymph nodes.

The sentinel lymph node is the first lymph node where cancer drains and could cause metastasis. This is the first step in metastatic cancer cell spread. The existence of tumor cells (lymphatic metastasis) in the sentinel node is considered a poor prognostic factor in patients with cancer. There is also lymphatic enlargement in the efferent and afferent lymph vessels of the sentinel lymph node (Stacker 2014, 164–165). This enlargement promotes the arrival of tumor cells in the sentinel node and in other regional lymph nodes. The description of these processes is very important because it implies the existence of structural changes not only in new lymphatic vessels but also in pre-existing lymphatics, changes which promote the spread of tumors.

TUMOR LYMPHANGIOGENESIS: CHEMOTAXIS

Over many years, the lymphatic system was thought to be a passive element in the development of tumor metastasis, and it was considered only as

a transport system. Recent studies, however, indicate that tumor cells are guided to the lymphatics via chemokines produced by the lymphatic endothelium (Podgrabinska 2014, 48).

Chemokines are a family of small cytokines or signaling proteins secreted by cells. This name derives from their ability to induce chemotaxis or movement of nearby sensitive cells. These molecules produce a chemokine gradient that facilitates the entry and transport of tumor cells within the lymphatic vessels. Therefore, tumor-associated lymphangiogenesis facilitates the mobilization of tumor cells into peritumoral lymphatic capillaries by means of chemotaxis. The proximity between tumor cells and lymphatic endothelial cells from new lymphatic capillaries encourages a response to chemokines derived from lymphatic endothelial cells (LECs).

Chemokine CXCL12 is upregulated on lymphatic vessels. This chemokine stimulates migration of tumor cells CXCR4/CD133 (tumor stem cells) to the vicinity of lymphatic endothelial cells (Stacker 2014, 164; Podgrabinska 2014, 48).

Mannose receptor and common lymphatic endothelial and vascular endothelial receptor-1 (CLEVER-1) are molecules that mediate lymphocyte adhesion to lymphatic vessels. MR and CLEVER-1 expressions were detected on lymphatic vessels, and both are associated with increased risk of lymph node metastasis (Podgrabinska 2014, 48).

The chemokine CC motif ligand 1 (CCL 1) is a small glycoprotein expressed in the subcapsular sinuses of lymph nodes. The lymphatic subcapsular sinus has been described as the first site of metastasis of tumor cells in lymph nodes. Chemokine CCL 1 attracts monocytes, NK cells, immature B cells, and dendritic cells through interaction with a cell surface chemokine receptor called CCR8. The activation CCL1–CCR8 controls the output of tumor cells to afferent lymphatics. Therefore, the subcapsular sinus lymphatic plays a key role in the entry of tumor cells into the lymphatic nodes (Podgrabinska 2014, 49; Stacker 2014, 164).

LYMPHATIC ENDOTHELIAL CELLS: IMMUNOREGULATORY ROLE IN CANCER

Lymphatic endothelial cells play an important role in the movement of immune cells from tissues into the lymphatic capillaries. Endothelial cells

lining the subcapsular sinuses present chemokines as CCL1, which attracts CCR8 receptor cells into the lymph node.

The chemokine CCL21 (produced by lymphatic endothelial cells) binds to the receptor CCR7, existing in some immune cells (dendritic cells, macrophages, and some T cell populations), to trigger their directed migration (Stacker 2014, 163).

Aside from regulating cellular traffic, lymphatic endothelial cells can modulate immune responses. The role of LECs in the control of immune cells could be an important factor to immune surveillance during the early stages of tumor development, as LECs may promote a protective immune response against cancer.

Conversely, LECs may also promote immunosuppression, which facilitates the immune escape of tumor cells and therefore their spread. The activation of LECs may also inhibit antitumor T CD 8+ cells, promoting the survival of tumor cells in the lymphatic system (Podgrabinska 2014, 50–51).

STEM CELLS AND TUMOR LYMPHANGIOGENESIS

Solid tumors comprise very heterogeneous subsets of cells. Among the different types of cells is a small group of tumor stem cells capable of self-renewal. These can also differentiate into different groups of tumor cells. Stem cells have a high resistance to therapeutic agents such as chemotherapy and radiation and are associated with high aggressiveness, development of metastatic foci, and lymphangiogenesis through various mechanisms.

First, tumor stem cells are involved in lymphangiogenesis by producing vascular endothelial growth factors. Aside from this, tumor stem cells may generate vascular mimicry, which produces endothelial cells similar to blood or lymphatic endothelial cells. Tumor stem cells can also develop epithelial–mesenchymal transition, which transform them into migrating cancer stem cells.

These migrating cancer stem cells have great mobility due to chemotaxis, allowing them to reach lymph nodes or distant metastases. The epithelial–mesenchymal transition of tumor stem cells is a major mechanism for the acquisition of the metastatic phenotype in carcinogenesis (Li 2015, 438, 441–443).

LYMPHATIC NODES AND DISTANT METASTASES

Lymph nodes are usually the first sites of detectable metastasis, which could be due to the preference of tumor cells to enter into lymphatic vessels. The lymph node acts as a filter where lymphocytes, macrophages, and antigen-presenting cells initiate a specific immune response. There are no explanations for why tumor cells have preferred routes for metastasis or what percentage of tumor cells can metastasize by each route. The lymphatics vessels contribute to the spread of cancer cells, firstly as a route for dissemination from the primary tumor to regional lymph nodes and secondly as a route for metastasis in distant organs.

From a therapeutic point of view, it is crucial that we understand the role of lymphangiogenesis in the formation and progression of distant metastasis. Experimental evidence has shown that inhibiting lymph node metastasis decreases the incidence of lung metastasis. Interestingly, by inhibiting lymphangiogenesis, it is possible to prevent the lymphatic spread of tumor cells without compromising tumor growth. Several experimental studies with animal models have shown that blocking the binding between VEGF-C and VEGFR3 could prevent the appearance of distant metastases (Podgrabinska 2014, 49–50).

CONCLUSION

Based on the events described, it is possible that the lymphatic pathway is the main route of distant tumor spread. Tumor cells penetrate more easily into lymphatic capillaries than blood capillaries. There are many factors that favor this, such as the following:

- The absence of a basal membrane in peritumoral lymphatic capillaries
- Structural changes in lymphatic vessels during lymphangiogenesis
- The facilitation of the entry of tumor cells into lymphatic vessels and their migration ability by chemotaxis
- The immunomodulatory role of lymphatic endothelial cells, which could facilitate the survival of tumor cells

Circulating tumor cells in the lymph system can reach systemic circulation and thus target organs. Instead, tumor-associated blood capillaries have

basement membranes, and they often collapse with aberrant distribution. In addition, blood endothelial cells lack immunomodulatory activity. This fact explains why primary brain tumors grow and increase in size while never metastasizing distantly. Indeed, brain tumors can spread to other sites in the brain or spine but rarely to distant organs.

This is due to the lack of lymphatic vessels within the brain. The central nervous system presents lymphatic vessels in the dural sinuses of the meninges, which are connected with deep cervical vessels. However, there are no lymphatic vessels or lymphatic endothelial cells inside the brain, and so there is no tumor lymphangiogenesis. Nevertheless, intense tumor angiogenesis facilitates tumor growth. This fact demonstrates the poor contribution of tumor-associated blood capillaries to the development of tumor metastasis.

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A.D.A.M. Interactive Anatomy online: student lab activity guide LCCN: 2012039437 Personal name: Schaeffer, Scott D. Main title: A.D.A.M. Interactive Anatomy online: student lab activity guide / Scott D. Schaeffer. Edition: 4th ed. Published/Created: Philadelphia: Wolters Kluwer Health/Lippincott Williams and Wilkins, c2014. Description: xvii, 196 p.: col. ill.; 28 cm. ISBN: 9781451120394 (pbk.: alk. paper) LC classification: QM32 .L34 2014 Variant title: ADAM Interactive Anatomy online Related names: Lafferty, Mark. A.D.A.M. Interactive Anatomy student lab guide. Contents: Skeletal system -- Muscular system -- Nervous system -- Special senses -- Endocrine system -- Cardiovascular system -- Lymphatic system -- Respiratory system -- Digestive system -- Urinary system -- Reproductive systems. Subjects: Problems and Exercises--Laboratory Manuals. Anatomy--Laboratory Manuals. Notes: Rev. ed. of: A.D.A.M. Interactive Anatomy student lab guide / Mark Lafferty, Samuel Panella. 3rd ed. c2005. Includes bibliographical references.

Anand's human anatomy for dental students LCCN: 2012471688 Personal name: Anand, Mahindra Kumar. Main title: Anand's human anatomy for dental students / Mahindra Kumar Anand. Published/Created: New Delhi, India: Jaypee Brothers Medical Publishers, 2012. Description: 752 p.: ill.; 28 cm. ISBN: 9350255030 9789350255032 Contents: 1. Introduction and anatomical terms - 2. Cell - 3. Tissues - 4. Organization of body - 5. Skeletal system and joints - 6. Muscular system - 7. Nervous system - 8. Cardiovascular system - 9. Blood and its components - 10. Lymphatic system - 11. Respiratory system - 12. Digestive system - 13. Urinary system - 14. Endocrine system - 15. Reproductive system - 16. Skin and its appendages - 17. Review of general and systemic anatomy - 18. Osteology of head

and neck - 19. Scalp and face - 20. Eye and orbit - 21. Dura mater, intra cranial venous sinuses - 22. Pituitary gland - 23. Temporal and infratemporal regions - 24. Parotid and submandibular regions - 25. Neck and its triangles - 26. Back of neck and the back - 27. Oral cavity - 28. Nose and paranasal sinuses - 29. Pharynx - 30. Larynx - 31. Ear - 32. Cervical viscera and deep muscles of neck - 17. Review of general and systemic anatomy - 18. Osteology of head and neck - 19. Scalp and face - 20. Eye and orbit - 21. Dura mater, intra cranial venous sinuses - 22. Pituitary gland - 23. Temporal and infratemporal regions - 24. Parotid and submandibular regions - 25. Neck and its triangles - 26. Back of neck and the back - 27. Oral cavity - 28. Nose and paranasal sinuses - 29. Pharynx - 30. Larynx - 31. Ear - 32. Cervical viscera and deep muscles of neck - 49. Endocrine system - 50. Review of histology - 51. Cell division - 52. Cytogenetics, chromosome and chromosomal abnormalities - 53. Molecular basis of genetics - 54. Review of genetics - 55. General embryology - 56. Development of musculoskeletal system - 57. Development of head and neck - 58. Development of nervous system - 59. Molecular regulation of development - 60. Review of embryology - 61. Radiological anatomy - 62. Anatomical basis of clinical examination. Subjects: Dentistry. Embryology, Human. Histology. Human anatomy.

Anatomy and physiology: foundations for the health professions LCCN: 2011040248 Personal name: Roiger, Deborah. Main title: Anatomy and physiology: foundations for the health professions / Deborah Roiger. Published/Created: New York, NY: McGraw-Hill, c2013. Description: 1 v. (various pagings): col. ill.; 28 cm. ISBN: 9780073402123 (alk. paper) 0073402125 (alk. paper) LC classification: QP34.5 .R65 2013 Variant title: Anatomy and physiology Contents: The basics -- Levels of organization of the human body -- The integumentary system -- The skeletal system -- The muscular system -- The nervous system -- The nervous system: senses -- The endocrine system -- The cardiovascular system: blood -- The cardiovascular system: heart and vessels -- The lymphatic system -- The respiratory system -- The digestive system -- The excretory/urinary system -- The male reproductive system -- The

female reproductive system. Subjects: Anatomy. Physiological Phenomena. Notes: Includes bibliographical references and index.

Anatomy, physiology and disease: foundations for the health professions LCCN: 2012027272 Personal name: Roiger, Deborah. Main title: Anatomy, physiology and disease: foundations for the health professions / Deborah Roiger, Nia Joyner Bullock. Published/Created: New York, NY: McGraw-Hill, c2014. Description: 1 v. (various pagings), 13 p. of plates: col. ill.; 28 cm. ISBN: 9780073402116 (alk. paper) 0073402117 (alk. paper) LC classification: QS18.2 R741 2014 Variant title: Anatomy, physiology, and disease Related names: Bullock, Nia Joyner. Contents: The basics -- Levels of organization of the human body -- Introduction to pathology -- The integumentary system -- The skeletal system -- The muscular system -- The nervous system -- The nervous system: senses -- The endocrine system -- The cardiovascular system: blood -- The cardiovascular system: heart and vessels -- The lymphatic system -- The respiratory system -- The digestive system -- The excretory/urinary system -- The male reproductive system -- The female reproductive system. Subjects: Anatomy--Examination Questions. Physiological Phenomena--Examination Questions. Pathology--Examination Questions. Notes: Includes index.

Applied anatomy and physiology for manual therapists LCCN: 2011030176 Personal name: Archer, Patricia A. Main title: Applied anatomy and physiology for manual therapists / Pat Archer, Lisa A. Nelson. Edition: 1st ed. Published/Created: Philadelphia: Wolters Kluwer/Lippincott Williams and Wilkins Health, c2013. Description: xxii, 453 p.: col. ill.; 28 cm. ISBN: 9781605476551 LC classification: QP34.5 .A73 2013 Variant title: Applied anatomy and physiology for manual therapists Related names: Nelson, Lisa A. Contents: Applying A and P to the practice of manual therapy -- The body and its terminology -- Chemistry, cells, and tissues -- Body membranes and the integumentary system -- The skeletal system -- The skeletal muscle system -- The nervous system -- Neuromuscular and

myofascial connections -- The endocrine system -- The cardiovascular system -- The lymphatic system -- Immunity and healing -- The respiratory system -- The digestive system -- The urinary system -- The reproductive system. Subjects: Musculoskeletal Manipulations--methods--Problems and Exercises. Musculoskeletal Physiological Phenomena--Problems and Exercises. Musculoskeletal System--anatomy and histology--Problems and Exercises. Notes: Includes bibliographical references and index.

Bates' nursing guide to physical examination and history taking LCCN: 2011027307 Personal name: Hogan-Quigley, Beth. Main title: Bates' nursing guide to physical examination and history taking / Beth Hogan-Quigley, Mary Louise Palm, Lynn S. Bickley. Published/Created: Philadelphia: Wolters Kluwer Health/Lippincott Williams and Wilkins, c2012. Description: xviii, 924 p.: col. ill.; 29 cm. ISBN: 9780781780698 (alk. paper) 0781780691 (alk. paper) LC classification: RC76 .H674 2012 Portion of title: Nursing guide to physical examination and history taking Related names: Palm, Mary Louise. Bickley, Lynn S. Bates, Barbara, 1928-2002. Contents: Introduction to health assessment -- Critical thinking in health assessment -- Interviewing and communication -- The health history -- Cultural and spiritual assessment -- Physical examination -- Beginning the physical examination: general survey, vital signs, and pain -- Nutrition -- The integumentary system -- The head and neck -- The eyes -- Ears, nose, mouth, and throat -- The respiratory system -- The cardiovascular system -- The peripheral vascular system and lymphatic system -- The gastrointestinal and renal systems -- The breasts and axillae -- The musculoskeletal system -- Mental status -- The nervous system -- Reproductive systems -- Putting it all together -- Assessing children: infancy through adolescence -- Assessing older adults. Subjects: Physical diagnosis. Medical history taking. Nursing assessment. Nursing Assessment. Medical History Taking. Physical Examination. Notes: Includes bibliographical references and index.

Biofluid mechanics: an introduction to fluid mechanics, macrocirculation, and microcirculation LCCN: 2011499693 Personal name: Rubenstein, David A. Main title: Biofluid mechanics: an introduction to fluid mechanics, macrocirculation, and microcirculation / David A. Rubenstein, Wei Yin, Mary D. Frame. Published/Created: Amsterdam; Boston: Elsevier Academic Press, c2012. Description: x, 400 p.: ill.; 24 cm. ISBN: 9780123813831 0123813832 LC classification: QP90.5 .R83 2012 Related names: Frame, Mary D. Yin, Wei, Ph.D. Contents: Fluid mechanics basics -- Fundamentals of fluid mechanics -- Conservation laws -- Macrocirculation -- Heart -- Blood flow in arteries and veins -- Microcirculation -- Microvascular beds -- Mass transport and heat transfer in the microcirculation -- Lymphatic system -- Other biologic flows within the body -- Flow in the lungs -- Intraocular fluid flow -- Lubrication of joints -- Flow through the kidney -- Modeling and experimental techniques -- In Silico biofluid mechanics -- In vitro biofluid mechanics -- In vivo biofluid mechanics. Subjects: Body fluid flow. Biological control systems. Body Fluids--physiology. Rheology. Biomechanics. Blood Circulation--physiology. Hemodynamics--physiology. Notes: Includes bibliographical references and index. Series: Academic Press series in biomedical engineering Academic Press series in biomedical engineering.

Body: [an amazing tour of human anatomy] LCCN: 2014395985 Main title: Body: [an amazing tour of human anatomy] / [written by Richard Walker]. Edition: 2014 ed. Published/Created: New York: Sandy Creek, 2014. Description: 96 p.: col. ill.; 31 cm ISBN: 9781435156845 (hc.) 1435156846 (hc.) LC classification: QP37 .B675 2014 Related names: Walker, Richard, 1951- DK Publishing, Inc. Summary: Text and colorful illustrations introduce the make up of the human body with cutaway drawings and explanations of the functions of the various body parts. -- Source other than Library of Congress. Contents: Introduction: Creating the images -- Body systems -- Skeletal system -- Muscular system -- Nervous system -- Cardiovascular system -- Endocrine system -- Lymphatic

system -- Skin, hair, and nails -- Head -- Head and neck -- Brain and spinal cord -- Skull and teeth -- Head muscles -- Tongue and nose -- Ear -- Eye -- Mouth and throat -- Upper body -- Thorax -- Heart -- Respiratory system -- Lungs -- Shoulder -- Arm and elbow -- Spine and back -- Trunk muscles -- Abdomen -- Digestive system -- Stomach -- Liver and gallbladder -- Intestines -- Pelvis -- Kidneys and bladder -- Female reproduction -- Male reproduction -- Lower body -- Hip -- Leg muscles -- Thigh -- Knee and lower leg -- Foot and ankle -- Glossary -- Index. Subjects: Human body--Juvenile literature. Human anatomy--Juvenile literature. Body, Human. Human anatomy. Human anatomy. Human body. Form/Genre: Juvenile works. Notes: Subtitle from cover. Includes index and glossary. "Copyright 2005, 2014 Dorling Kindersley Limited" "An imprint of Sterling Publishing"

Case studies in microbiology: a personal approach LCCN: 2011037190 Personal name: Anderson, Rodney P. Main title: Case studies in microbiology: a personal approach / Rodney Anderson, Linda Young. Published/Created: Hoboken, NJ: Wiley, c2012. Description: x, 144 p.: ill. (chiefly col.); 28 cm. Links: Cover image http://catalogimages.wiley.com/images/db/jimages/9780470631225.jpg ISBN: 9780470631225 (pbk.) 0470631228 (pbk.) LC classification: QR41.2 .A53 2012 Related names: Young, Linda, 1961- Summary: "This first edition text developed and evolved to meet three pedagogical goals we deemed essential for those studying allied health and are pre-professional. The use of microbiology case studies were modified to maintain their value as tools that result in critical thinking and knowledge retention while providing a more realistic context for preparing future health care professionals. Consequently, the text has real life, personally-oriented microbiology cases appropriate for those in nursing, pharmacy, and other allied health disciplines (pre-med, pre-PA, CLS, etc.). This format presents material as a story about the patient as well as information regarding their family circumstances, personal characteristics, and individual motivations"--Provided by publisher. Subjects: Microbiology--Case studies. Microbiology--Case Reports.

Microbiology--Examination Questions. Clinical Medicine--methods--Case Reports. Clinical Medicine--methods--Examination Questions. Microbiological Phenomena--Case Reports. Microbiological Phenomena--Examination Questions. Notes: Machine generated contents note: I. Community-Acquired Infections.A. Skin, Eyes and Underlying Tissues.1. Boils Staphylococcus aureus (MSSA): A Homeless Hazard.2. Impetigo Staphylococcus aureus (MRSA): The Funk.3. Folliculitis Staphyolococcus aureus (MRSA): Hats Off to MRSA.4. Osteomyelitis Polymicrobial Infection: Trouble is Afoot.5. Necrotizing Fasiitis Streptococcus pyogenes: Down on the Farm.6. Viral Conjunctivitis Adenovirus: My What Pretty Eyes You Have!7. Post-operative osteomyelitis Pseudomonas aeruginosa: He Did It His Way.8. Dermatophytic Fungi Tiichophyton: The Tat Is Where It's At.9. Cellulitis Staphylococcus epidermidis: A Persistent Pimple.B. Nervous System.1. Meningococcal Meningitis Neisseria meningitides: Life in the Meningitis Belt.2. Rabies Rabies Virus: The Flying Mouse.3. West Nile Fever West Nile Virus: Vacation Headaches.C. Cardiovascular and Lymphatic System.1. Sepsis Streptococcus pneumoniae: A Common Opportunistic Pathogen.2. Rheumatic Fever Streptococcus pyogenes: Unhappy Returns.3. Tularemia Fransicella tularensis: Bunny Bits.4. Rocky Mountain Spotted Fever Rickettsia rickettsii: The Black Measles.5. Mononucleosis Epstein Barr Virus: Pucker Up.6. Toxoplasmosis Toxoplasma gondii: Toxoplamosis-Don't Blame Fluffy.D. Respiratory System.1. Strep Throat and Scarlet Fever Streptococcus pyogenes: Strawberry Red.2. Influenza Influenza A Virus (H1N1): An Evolving Situation.3. Q Fever Coxiella burnetii: Q Fever-An Occupational Hazard.4. Viral Pharyngitis Adenovirus: Swimming Pool Blues.E. Digestive System.1. Shigellosis Shigella sonnei: Hand Washing ABCs.2. Clostridium difficile-Associated Diarrhea Clostridium dificile: A Distressing Side Effect.3. Hepatitis A Hepatitis A Virus: Hold the Onions.4. Viral Gastroenteritis Norovirus: Diarrhea 101.5. Giardiasis Giardia lamblia: An Uninvited Party Guest.F. Urinary and Reproductive Systems. 1.

Cystitis Escherichia coli: The Honeymoon Is Over. 2. Gonorrhea Neisseria gonorrheae: Sex, Drugs and Rock and Roll! 3. Genital Herpes Herpes Simplex Virus Type II: A Bad First Impression. 4. Genital Warts and Cervical Cancer Human Papilloma Virus: The Domino Effect. 5. Candidiasis Candida albicans: An Ongoing Problem. 6. Trichomoniasis Trichomonas vaginalis: An Infectious New Lifestyle.II. Nosocomial Infections. 1. Toxic Shock Syndrome Staphylococcus aureus TSS toxin: A Nose for Trouble. 2. Hepatitis C Hepatitis C Virus: A Hep C History Lesson. 3. Septecemia Staphylococcus aureus: The Super Bug.III. Family Health Care.A. Pediatric Infections. 1. Fifth's Disease Human Parvovirus B19: A New Twist on a Childhood Disease. 2. Chicken Pox Varicella Zoster Virus: Why Did the Chicken Cross the Road? 3. Hand Foot and Mouth Disease Coxsackie Virus A17: Hand, Foot and Mouth Disease. 4. Scarlet Fever Streptococcus pyogenes: Seeing Red. 5. Bronchiolitis Respiratory Syncytial Virus: 'Tis the Season. 6. Swimmer's Ear: Pseudomonas aeruginosa: Splash.B. Childbearing-Related Infections. 1. Group B Strep Colonization Streptococcus agalactiae: Special Delivery 2. Listeriosis Listeria monocytogenes: A Cookout Concern.C. Geriatric Infections. 1. Shingles Varicella Zoster Virus: The Second Time Around. 2. Gonorrhea: Neisseria gonorrheae: An Unexpected Outbreak.IV. Food Safety. 1.Staphylococcal Food Poisoning Staphylococcus aureus enterotoxin: No Thanks, I'll Have the Turkey. 2. Bacterial Meningitis Enterobacter sakazaki: Danger in the NICU.V. Regionally-Acquired Infections. 1. Lyme Disease Borrellia burgdorferi: An Infectious Vacation. 2. Hanta Virus Pulmonary Syndrome Sin Nombre Virus: Rain, Rain, Go Away.

Dental terminology LCCN: 2011942787 Personal name: Dofka, Charline M. Main title: Dental terminology / Charline Dofka. Edition: 3rd ed. Published/Created: Clifton Park, NY: Delmar, Cengage Learning, c2013. Description: xvi, 464 p.: ill (chiefly col.); 23 cm. ISBN: 9781133019718 (pbk.) 1133019714 (pbk.) LC classification: RK28 .D64 2013 Contents: 1. Introduction to dental terminology: Locate the dental word; Pronounce the

dental word; Analyze the structure of the dental word; Define the meaning of the dental word; Pluralize the dental word; Use the dental word; Review exercises -- 2. Anatomy and oral structures: Anatomy of the skull; Anatomical features of the skull; Landmarks and features of the mandible; Muscles of mastication; Trigeminal nerve location and functions; Blood supply of the cranium; Locations and purposes of the salivary glands; Agents and functions of the lymphatic system; Important structures in the oral cavity; Review exercises -- 3. Tooth origin and formation: Classification of the human dentition; Histological stages of tooth development; Tissue structure of the teeth; Tissue composition of the periodontium; Odontology/morphology; Tooth surfaces; Review exercises -- 4. Practice and facility setups: Dental professionals; Places of employment; Dental hand instruments; Rotary dental instruments; Dental facility operative equipment; Review exercises -- 5. Infection control: Disease conditions; Causes of disease and infection; Port of entry for disease; Immunity factors; Disease prevention; Agencies concerned with disease control; Review exercises -- 6. Emergency care: Emergency-prevention techniques; Emergency-prevention equipment and materials; Airway obstruction and resuscitation protocol; Classification of shock; Common medical emergencies; Common dental emergencies; Review exercises -- 7. Examination and prevention: Procedures involved with the initial examination; Examination of the oral tissues; Examination of the teeth; Charting methods; Alginate impressions; Home preventive techniques; Dental facility preventive practices; Review exercises -- 8. Pain management and pharmacology: Description of pain and methods to relieve distress; Local anesthesia; General anesthesia; Pharmacology and the science of drugs; Drug interactions with body functions; Drug forms and methods of distribution; Routes for drug administration; Drug prescription content; Classification and types of drug agents; Review exercises -- 9. Radiography: Definition and production of X-rays; Properties of roentgen rays; Measurement of radiation energy; Radiation protection; Composition, types, and qualities of dental radiographs; Techniques for

exposing radiographs; Radiographic film processing; Digital image retrieval and enhancement; Mounting radiographs; Assorted radiographic errors; 3D radiology; Review exercises -- 10. Tooth restorations: Patient preparation and procedure area; Isolation of the operative site; Preparation of the restorative site; Matrix placement; Cements, liners, and base materials; Restoration placement terminology; Restorative materials; Finishing methods; Review exercises -- 11. Cosmetic dentistry: Definition of cosmetic dentistry and related areas; Smile makeover; Tooth whitening; Tooth bonding and veneer application; Cosmetic tooth restorations; Periodontal tissue surgery; Dental implants; Accelerated orthodontics; Review exercises -- 12. Prosthodontics: Divisions in the field of prosthodontics; Types and characteristics of prosthodontic materials; Fixed prosthodontics; Removable dental prostheses; Procedures and methods used in the prosthodontic practice; Use of implants in prosthodontics; Miscellaneous prosthodontic services; Review exercises -- 13. Endodontics: Science and practice of endodontic dentistry; Diagnostic procedures to determine pulpal conditions; Endodontic treatment procedures; Endodontic treatment equipment and materials; Surgical endodontic treatments; Endodontic treatment of traumatized teeth; Tooth replantation procedures; Review exercises -- 14. Oral and maxillofacial surgery: Duties and functions of an oral and maxillofacial surgeon; Instrumentation related to oral surgery; Surgical procedures involved in exodontia; Procedures involved in soft-tissue surgery; Procedures involved in minor bone surgery; Surgical procedures involved in fracture repair; Procedures involved in maxillofacial surgery; Oral surgery procedures involved with TMJ dysfunction; Surgical procedures involved in implantology; Oral surgery role in esthetic dentistry; Review exercises -- 15. Orthodontics: Purpose of orthodontic practice and malocclusion classifications; Types and methods of orthodontic treatment; Requirements for diagnosis and treatment planning for malocclusion; Intraoral appliances and auxiliaries used in orthodontics; Types and purposes of headgear and traction devices; Assorted and

specialized appliances and retainers; Instrumentation for the orthodontic practice; Review exercises -- 16. Periodontics: Anatomy of the periodontium; Etiology and symptoms of periodontal diseases; Classification of periodontal diseases; Periodontal examination and evaluation; Measurement and recording of periodontal conditions; Periodontial treatment methods; Periodontal involvement with dental implants and cosmetic dentistry; Instrumentation for periodontics; Review exercises -- 17. Pediatric dentistry: Scope of pediatric dentistry; Development and growth concerns of the pediatric dentition; Maintenance and preservation of the pediatric dentition; Restorative dental care for the primary dentition; Control and sedation of the child patient; Treatment for trauma and abuse; Use of dental records for patient identification; Miscellaneous child health conditions; Review exercises -- 18. Dental laboratory materials: Impression materials; Gypsum materials; Wax materials; Dental polymer materials; Precious and base metals; Abrasive and polishing materials; Cement materials; Characteristics of dental laboratory materials; Review exercises -- 19. Dental laboratory procedures: Range and scope of the dental laboratory; Dental laboratory equipment; Denture construction laboratory procedures; Removable partial denture construction laboratory procedures; Fixed prosthodontic dental laboratory procedures; Miscellaneous dental laboratory procedures; CAD/CAM in the dental laboratory; Review exercises -- 20. Business management procedures: Office communication procedures; Appointment control; Patient records and filing procedures; Business correspondence; Dental insurance terms; Financial management; Inventory control; Legal and ethical terms; Review exercises -- Appendixes: A. Word elements; B. Answers to chapter 1 exercises -- Glossary -- Glossary of acronyms -- Glossary of insurance terms. Subjects: Dentistry--Terminology--Textbooks. Dentistry--Programmed instruction. Dentistry--Terminology--English. Notes: Includes index.

Elegant anatomy: the eighteenth-century Leiden anatomical collections LCCN: 2014033549 Personal name: Hendriksen,

Marieke M. A. Main title: Elegant anatomy: the eighteenth-century Leiden anatomical collections / by Marieke M.A. Hendriksen.
Published/Produced: Leiden; Boston: Brill, [2015]
Description: xi, 249 pages: illustrations; 25 cm. ISBN: 9789004262782 (hardback: acid-free paper) 9004262784 (hardback: acid-free paper) LC classification: QM51.N42 L34 2015 Scope and content: "In Elegant Anatomy Marieke Hendriksen offers an account of the material culture of the eighteenth-century Leiden anatomical collections, which have not been studied in detail before. The author introduces the novel analytical concept of aesthesis, as these historical medical collections may seem strange, and undeniably have a morbid aesthetic, yet are neither curiosities nor art. As this book deals with issues related to the keeping and displaying of historical human remains, it is highly relevant for material culture and museum studies, cultural history, the history of scientific collections and the history of medicine alike. Unlike existing literature on historical anatomical collections, this book takes the objects in the collections as its starting point, instead of the people that created them"--From publisher's website. Contents: Introduction: Understanding eighteenth-century Leiden anatomy -- Elegant anatomy: aesthesis -- Quicksilver anatomy: exploring the lymphatic system with mercury -- Hands, lace and plants: meaningful embellishments -- Beautiful monsters: how deformity can be elegant -- Colonial bodies: collecting the exotic other -- Back to the bone: the end of aesthesis -- Conclusion: Aesthesis and the future of historical anatomical collections. Subjects: Anatomical museums--Netherlands--Leiden--History--18th century. Human anatomy--Netherlands--Leiden--History--18th century. Human anatomy--Netherlands--Leiden--Methodology--History--18th century. Human body--Social aspects--Netherlands--Leiden--History--18th century. Material culture--Netherlands--Leiden--History--18th century. Senses and sensation--Social aspects--Netherlands--Leiden--History--18th century. Aesthetics--Social aspects--Netherlands--Leiden--History--18th century. Art and science--Netherlands--Leiden--History--18th century. Leiden (Netherlands)--Intellectual life--18th century. Notes: Includes

bibliographical references (pages 215-242) and index. Series: History of science and medicine library, 1872-0684; volume 47

Essentials of anatomy and physiology LCCN: 2014012086 Personal name: Scanlon, Valerie C., 1946- author. Main title: Essentials of anatomy and physiology / Valerie C. Scanlon, Tina Sanders. Edition: Seventh edition. Published/Produced: Philadelphia, PA: F. A. Davis, [2015] Description: xviii, 669 pages; 26 cm ISBN: 9780803639577 LC classification: QP34.5 .S288 2015 Related names: Sanders, Tina, 1943- author. Contents: Organization and general plan of the body -- Some basic chemistry -- Cells -- Tissues and membranes -- The integumentary system -- The skeletal system -- The muscular system -- The nervous system -- The senses -- The endocrine system -- Blood -- The heart -- The vascular system -- The lymphatic system and immunity -- The respiratory system -- The digestive system -- Body temperature and metabolism -- The urinary system -- Fluid-electrolyte and acid-base balance -- The reproductive systems -- Human development and genetics -- An introduction to microbiology and human disease. Subjects: Anatomy. Physiological Phenomena. Notes: Includes index.

Essentials of human anatomy and physiology LCCN: 2010041190 Personal name: Marieb, Elaine Nicpon, 1936- Main title: Essentials of human anatomy and physiology / Elaine N. Marieb. Edition: 10th ed. Published/Created: San Francisco, CA: Benjamin Cummings, c2012. Description: xxiv, 632 p.: col. ill.; 28 cm. + 1 CD-ROM (4 3/4 in.) ISBN: 9780321695987 (student edition: alk. paper) 0321695984 (student edition: alk. paper) 9780321714824 (professional copy: alk. paper) 0321714822 (professional copy: alk. paper) 9780321707284 (pbk. with CD-ROM) 0321707281 (pbk. with CD-ROM) LC classification: QP34.5 .M455 2012 Variant title: Essentials of human anatomy and physiology Contents: The human body: an orientation -- Basic chemistry -- Cells and tissues -- Skin and body membranes -- The skeletal system -- The muscular system -- The nervous system -- Special senses -- The endocrine system -- Blood -- The cardiovascular system -- The lymphatic system

and body defenses -- The respiratory system -- The digestive system and body metabolism -- The urinary system -- The reproductive system. Subjects: Human physiology. Human anatomy. Anatomy. Physiological Phenomena. Notes: LC copy 2 imperfect: accompanying CD-ROM wanting. Includes bibliographical references and index.

Health assessment in nursing LCCN: 2013020582 Personal name: Weber, Janet, author. Main title: Health assessment in nursing / Janet R. Weber, Professor, Director RN-BSN Program, Department of Nursing, Southeast Missouri State University, Cape Girardeau, Missouri, Jane H. Kelley, Adjunct Professor, School of Nursing, Indiana Wesleyan University, Louisville, Kentucky. Edition: Fifth edition. Published/Produced: Philadelphia: Wolters Kluwer Health/Lippincott Williams and Wilkins, [2014] Description: xi, 900 pages: illustrations; 29 cm. ISBN: 9781451142808 (alk. paper) LC classification: RT48 .W43 2014 Related names: Kelley, Jane, 1944- author. Summary: "Health Assessment in Nursing, 5e provides all of the background needed for interviewing the client and performing assessment making this the perfect text for students learning Assessment. The unique 3-column format used for teaching students assessment techniques (Assessment Procedures/Normal Findings/Abnormal Findings) breaks the process down into easy-to-understand units. The COLDSPA mnemonic (Character, Onset, Location, Duration, Severity, Pattern, and Associated factors) provides logical structure for the patient interview helping students to remember the most essential questions to ask a client. A new chapter "Psychosocial, Cognitive, and Moral Development" focuses on those areas of development for young adults, middle-age adults, and older adutls ensuring that the nurse will perform a holistic nursing assessment. New integrated case study guides students through the assessment process helping them to develop the diagnostic reasoning skills every nurse needs. New Evidence-Based Practice Health Promotion and Disease Prevention boxes include Healthy People 2020 goals ensuring best practice. The new art program and interior design

enhance readability allowing students to develop the necessary skills needed to perform accurate and timely health assessments"--Provided by publisher. Contents: Machine generated contents note: Unit 1: Nursing Data Collection, Documentation, and Analysis Chapter 1. Nurse's Role in Health Assessment: Collecting and Analyzing Data Chapter 2. Collecting Subjective Data: The Interview and Health History Chapter 3. Collecting Objective Data: The Physical Examination Chapter 4. Validating and Documenting Data Chapter 5. Thinking Critically to Analyze Data and Make Informed Nursing Judgments Unit 2: Integrative Holistic Nursing Assessment Chapter 6. Assessing Mental Status and Substance Abuse Chapter 7. Assessing Psychosocial, Cognitive, and Moral Development Chapter 8. Assessing General Status and Vital Signs Chapter 9. Assessing Pain: The 5th Vital Sign Chapter 10. Assessing for Violence Chapter 11. Assessing Culture Chapter 12. Assessing Spirituality and Religious Practices Chapter 13. Assessing Nutritional Status Unit 3: Nursing Assessment of Physical Systems Chapter 14. Assessing Skin, Hair, and Nails Chapter 15. Assessing Head and Neck Chapter 16. Assessing Eyes Chapter 17. Assessing Ears Chapter 18. Assessing Mouth, Throat, Nose, and Sinuses Chapter 19. Assessing Thorax and Lungs Chapter 20. Assessing Breasts and Lymphatic System Chapter 21. Assessing Heart and Neck Vessels Chapter 22. Assessing Peripheral Vascular System Chapter 23. Assessing Abdomen Chapter 24. Assessing Musculoskeletal System Chapter 25. Assessing Neurological System Chapter 26. Assessing Male Genitalia and Rectum Chapter 27. Assessing Female Genitalia and Rectum Chapter 28. Pulling It All Together: Integrated Head-to-Toe Assessment Unit 4: Nursing Assessment of Special Groups Chapter 29. Assessing Childbearing Women Chapter 30. Assessing Newborns and Infants Chapter 31. Assessing Children and Adolescents Chapter 32. Assessing the Elderly Chapter 33. Assessing Families Chapter 34. Assessing Communities Subjects: Nursing Assessment--methods. Notes: Includes bibliographical references and index.

Hinman's atlas of urosurgical anatomy LCCN: 2012008133 Personal name: MacLennan, Gregory T. Main title: Hinman's atlas of urosurgical anatomy / Gregory T. MacLennan. Edition: 2nd ed. Published/Created: Philadelphia: Elsevier/Saunders, c2012. Description: xi, 368 p.: ill. (chiefly col.); 32 cm. ISBN: 9781416040897 (hardback) 1416040897 (hardback) LC classification: QM401 .H56 2012 Variant title: Atlas of urosurgical anatomy Related names: Hinman, Frank, 1915- Atlas of urosurgical anatomy. Contents: Venous system -- Lymphatic system -- Peripheral nervous system -- Skin -- Gastrointestinal tract -- Anterolateral body wall -- Posterolateral and posterior body wall -- Inguinal region -- Pelvis -- Perineum -- Organs -- Kidney, ureter, and adrenal glands -- Bladder, ureterovesical junction, and rectum -- Prostate and urethral sphincters -- Female genital tract and urethra -- Penis and male urethra -- Testis. Subjects: Urogenital System--anatomy and histology--Atlases. Notes: Rev. ed. of: Atlas of urosurgical anatomy / Frank Hinman Jr. c1993. Includes index.

Histology and cell biology: an introduction to pathology LCCN: 2011004748 Personal name: Kierszenbaum, Abraham L. Main title: Histology and cell biology: an introduction to pathology / Abraham L. Kierszenbaum, Laura L. Tres. Edition: 3rd ed. Published/Created: Philadelphia, PA: Saunders, c2012. Description: xiv, 701 p.: col. ill.; 28 cm. ISBN: 9780323078429 (alk. paper) LC classification: RB25 .K54 2012 Related names: Tres, Laura L. Contents: Epithelium -- Epithelial glands -- Cell signaling -- Connective tissue -- Osteogenesis -- Blood and hematopoiesis -- Muscle tissue -- Nervous tissue -- Sensory organs: vision and hearing -- Immune-lymphatic system -- Integumentary system -- Cardiovascular system -- Respiratory system -- Urinary system -- Upper digestive segment -- Lower digestive segment -- Digestive glands -- Neuroendocrine system -- Endocrine system -- Spermatogenesis -- Sperm transport and maturation -- Follicle development and the menstrual cycle -- Fertilization, placentation, and lactation. Subjects: Histology, Pathological. Pathology, Cellular. Histology. Cell

Biology. Pathology. Notes: Includes bibliographical references and index.

Human anatomy and physiology LCCN: 2012948429 Personal name: Van De Graaff, Kent M. (Kent Marshall), 1942- Uniform title: Schaum's outlines human anatomy and physiology Main title: Human anatomy and physiology / Kent M. Van De Graaff, PhD, Professor of Zoology, Weber State University, R. Ward Rhees, PhD, Professor of Zoology, Brigham Young University, Sidney L. Palmer, PhD, Chair, Department of Biology, Brigham Young University--Idaho. Edition: Fourth edition. Published/Produced: New York: McGraw-Hill Education, [2013] Description: ix, 414 pages: illustrations; 28 cm. ISBN: 9780071810791 007181079X LC classification: QP41 .V36 2013 Variant title: At head of title: Schaum's outlines Spine title: Schaum's outlines human anatomy and physiology Related names: Rhees, R. Ward. Palmer, Sidney. Contents: Introduction to the human body -- Cellular chemistry -- Cell structure and function -- Tissues -- Integumentary system -- Skeletal system -- Muscle tissue and mode of contraction -- Muscular system -- Nervous tissue -- Central nervous system -- Peripheral and autonomic nervous systems -- Sensory organs -- Endocrine system -- Cardiovascular system: blood -- Cardiovascular system: the heart -- Cardiovascular system: vessels and blood circulation -- Lymphatic system and body immunity -- Respiratory system -- Digestive system -- Metabolism, nutrition, and temperature regulation -- Urinary system -- Water and electrolyte balance -- Reproductive system. Subjects: Human physiology--Outlines, syllabi, etc. Human physiology--Problems, exercises, etc. Human anatomy--Outlines, syllabi, etc. Human anatomy--Problems, exercises, etc. Notes: Includes index. Series: Schaum's outline series

Illustrated anatomy of the head and neck LCCN: 2011043758 Personal name: Fehrenbach, Margaret J. Main title: Illustrated anatomy of the head and neck / Margaret J. Fehrenbach, Susan W. Herring. Edition: 4th ed. Published/Created: St. Louis, Mo.: Elsevier/Saunders, c2012. Description: ix, 317 [14] p.: col. ill.; 28 cm. ISBN: 9781437724196 (pbk.: alk.

paper) LC classification: QM535 .F44 2012 Related names: Herring, Susan W. Contents: Introduction to head and neck anatomy -- Surface anatomy -- Skeletal system -- Muscular system -- Temporomandibular joint -- Vascular system -- Glandular tissue -- Nervous system -- Anatomy of local anesthesia -- Lymphatic system -- Fasciae and spaces -- Spread of infection. Subjects: Head--anatomy and histology--Programmed Instruction. Neck--anatomy and histology--Programmed Instruction. Notes: Includes bibliographical references and index.

Immunology of the lymphatic system LCCN: 2013938836 Personal name: Santambrogio, Laura. Main title: Immunology of the lymphatic system / Laura Santambrogio, editor. Published/Produced: New York: Springer, [2013] Description: v, 177 pages: illustrations (some color); 24 cm Links: Publisher description http://www.loc.gov/catdir/enhancements/fy1314/2013938836-d.html Table of contents only http://www.loc.gov/catdir/enhancements/fy1314/2013938836-t.html ISBN: 9781461432340 (acid-free paper) 9781461432357 (ebk.) LC classification: QP115 .S26 2013 Related names: Santambrogio, Laura, editor of compilation. Subjects: Lymphatics--Immunology. Notes: Includes bibliographical references and index.

Introduction to anatomy and physiology LCCN: 2011920150 Personal name: Rizzo, Donald C. Main title: Introduction to anatomy and physiology / Donald C. Rizzo. Edition: 1st ed. Published/Created: Clifton Park, NY: Delmar, c2012. Description: xxix, 530 pages: col. ill.; 29 cm + 1 CD-ROM (4 3/4 in.) Links: Publisher description http://www.loc.gov/catdir/enhancements/fy1212/2011920150-d.html Table of contents only http://www.loc.gov/catdir/enhancements/fy1212/2011920150-t.html ISBN: 9781111138448 (hbk.) 1111138443 (hbk.) LC classification: QP34.5 .R554 2012 Contents: The human body -- The chemistry of life -- Cell structure -- Cellular metabolism and reproduction: mitosis and meiosis -- Tissues -- The integumentary system -- The skeletal system -- The articular system -- The muscular system -- The nervous system: introduction, spinal cord, and spinal nerves -- The nervous

system: the brain, cranial nerves, autonomic nervous system, and the special senses -- The endocrine system -- The blood -- The cardiovascular system -- The lymphatic system -- Nutrition and the digestive system -- The respiratory system -- The urinary system -- The reproductive system. Subjects: Human physiology--Textbooks. Human anatomy--Textbooks. Notes: Includes index.

Laboratory activity guide for anatomy and physiology LCCN: 2011049269 Personal name: Kipp, Brian H. Main title: Laboratory activity guide for anatomy and physiology / Brian H. Kipp. Published/Created: Philadelphia: Wolters Kluwer Health/Lippincott Williams and Wilkins, c2012. Description: ix, 201 p.: ill. (some col.); 28 cm. ISBN: 9781608312122 (pbk.: spiral bound) LC classification: QP44 .K55 2012 Contents: General laboratory safety -- Introduction to human anatomy -- Cellular anatomy and the microscope -- Osmosis and diffusion -- Basic histology -- The integumentary system -- The skeletal system -- The muscular system -- The nervous system -- The cardiovascular system -- The lymphatic system -- The respiratory system -- The endocrine system -- The digestive system -- The urinary system -- The male and female reproductive systems. Subjects: Anatomy--Laboratory Manuals. Physiological Phenomena--Laboratory Manuals. Notes: Includes bibliographical references and index.

Lippincott's textbook for nursing assistants: a humanistic approach to caregiving LCCN: 2010037710 Personal name: Carter, Pamela J. Main title: Lippincott's textbook for nursing assistants: a humanistic approach to caregiving / Pamela J. Carter. Edition: 3rd ed. Published/Created: Philadelphia: Wolters Kluwer Health/Lippincott Williams and Wilkins, c2012. Description: xxxiii, 862 p.: col. ill.; 28 cm. + 1 CD-ROM (4 3/4 in.) ISBN: 9781605476353 (alk. paper) 1605476358 (alk. paper) LC classification: RT84 .C375 2012 Portion of title: Textbook for nursing assistants Summary: Product Description: This textbook for nursing assistants will prepare students not only to function in the traditional nursing assistant role in nursing homes, hospitals, and home health, but also will prepare students to advance their careers. A nursing assistant student who

uses this text will have a firm foundation by which to transition to an LPN and ultimately an RN role. The text offers a compelling art program, a direct, conversational writing style, and an emphasis on professionalism and humanism. A back-of-book CD-ROM includes an audio glossary. Contents: Unit 1: Introduction To Health Care -- Chapter 1: Health care system -- Health care delivery, past and present -- Health care organizations -- Types of health care organizations -- Structure of health care organizations -- Oversight of a the health care system -- Ensuring quality health care -- Protecting health care workers -- Paying for health care -- Private and group insurance -- Medicare -- Medicaid -- Chapter 2: Nursing assistant -- Nursing, past and present -- Education of the nursing assistant -- OBRA requirements for certification -- Responsibilities of the nursing assistant -- Nursing team -- Delegation -- Chapter 3: Professionalism and job-seeking skills -- What is a professional? -- What is a work ethic? -- Punctuality -- Reliability -- Accountability -- Conscientiousness -- Courtesy and respectfulness -- Honesty -- Cooperativeness -- Empathy -- Desire to learn -- Personal health and hygiene -- Maintaining your physical health -- Maintaining your emotional health -- Personal hygiene and appearance -- Job-seeking skills -- Defining the ideal job -- Finding job openings -- Preparing resumes, cover letters, and reference lists -- Submitting applications -- Going on interviews -- Leaving a job -- Chapter 4: Legal and ethical issues -- Patients' and residents' rights -- Patients' rights -- Residents' rights -- Advance directives -- Laws: a way of preserving patients' and residents' rights -- Violations of civil law -- Violations of criminal law-abuse -- Ethics: guidelines for behavior -- Professional ethics -- Personal ethics -- Chapter 5: Communication skills -- What is communication? -- Communicating effectively -- Tactics that enhance communication -- Blocks to effective communication -- Conflict resolution -- Telephone communication -- Communication among members of the health care team -- Reporting -- Recording -- Nursing process -- Chapter 6: Those we care for -- Patients, residents, and clients -- Growth

and development -- Infancy (birth to 1 year) -- Toddlerhood (1 to 3 years) -- Preschool (3 to 5 years) -- School-age (5 to 12 years) -- Adolescence (12 to 20 years) -- Young adulthood (20 to 40 years) -- Middle adulthood (40 to 65 years) -- Later adulthood (65 to 75 years) -- Older adulthood (75 years and beyond) -- Basic human needs -- Maslow's hierarchy of human needs -- Human sexuality and intimacy -- Culture and religion -- Quality of life -- Person's family -- Unit 2: Safety -- Chapter 7: Communicable disease and infection control -- What is a microbe? -- Bacteria -- Viruses -- Fungi -- Parasites -- Defenses against communicable disease -- Immune system -- Antibiotics -- Communicable disease and the chain of infection -- Infection control in the health care setting -- Medical asepsis -- Surgical asepsis -- Barrier methods -- Isolation precautions -- Standard precautions -- Transmission-based precautions -- Procedure 7-1: Handwashing (hand hygiene) -- Procedure 7-2: Removing gloves -- Procedure 7-3: Putting on a gown -- Procedure 7-4: Removing a gown -- Procedure 7-5: Putting on and removing a mask -- Procedure 7-6: Removing more than one article of personal protective equipment (PPE) -- Procedure 7-7: Double-bagging (two assistants) -- Chapter 8: Bloodborne and airborne pathogens -- Bloodborne diseases -- Bloodborne transmission -- Hepatitis and HIV/AIDS -- Protecting yourself from bloodborne diseases -- Airborne diseases -- Airborne transmittal -- Tuberculosis (TB) -- Protecting yourself from airborne diseases -- Chapter 9: Workplace safety -- Protecting your body -- Ergonomics -- ABCs of good body mechanics -- Lifting and back safety -- Following procedures -- Preventing falls -- Preventing chemical injuries -- Preventing electrical shocks -- Fire safety -- Preventing fires -- Reacting to a fire emergency -- Disaster preparedness -- Workplace violence -- Chapter 10: Patient safety and restraint alternatives -- Accidents and incidents -- Risk factors -- Avoiding accidents -- Reporting accidents and incidents -- Restraints -- Use of restraints -- Complications associated with restraint use -- Restraint alternatives -- Applying restraints -- Procedure 10-1: Applying a vest restraint -- Procedure 10-2: Applying wrist or ankle restraints -- Procedure 10-3: Applying lap or waist

(belt) restraints -- Chapter 11: Positioning lifting, and transferring patients and residents -- Positioning patients and residents -- Basic positions -- Repositioning a person -- Transferring patients and residents -- Transferring a person to and from a wheelchair or chair -- Transferring a person to and from a stretcher -- Transferring a person using a mechanical lift -- Assisting a person with walking (ambulating) -- Procedure 11-1: Moving a person to the side of the bed (one assistant) -- Procedure 11-2: Moving a person to the side of the bed (two assistants) -- Procedure 11-3: Moving a person up in bed (one assistant) -- Procedure 11-4: Moving a person up in bed (two assistants) -- Procedure 11-5: Raising a person's head and shoulders -- Procedure 11-6: Turning a person onto his or her side -- Procedure 11-7: Logrolling a person (two assistants) -- Procedure 11-8: Applying a transfer (gait) belt -- Procedure 11-9: Transferring a person from a bed to a wheelchair (one assistant) -- Procedure 11-10: Transferring a person from a bed to a wheel (two assistants) -- Procedure 11-11: Transferring a person from a wheelchair to a bed -- Procedure 11-12: Transferring a person from a bed to a stretcher (four assistants) -- Procedure 11-13: Transferring a person from a stretcher to a bed (four assistants) -- Procedure 11-14: Transferring a person using a mechanical lift (two assistants) -- Procedure 11-15: Assisting a person with sitting on the edge of the bed ("dangling") -- Procedure 11-16: Assisting a person with walking (ambulating) -- Chapter 12: Basic first aid and emergency care -- Responding to an emergency -- Basic life support (BLS) measures -- Emergency situations -- Heart attacks and strokes -- Fainting (syncope) -- Seizures -- Hemorrhage -- Shock -- Airway obstructions (chocking) -- Chain of survival -- Procedure 12-1: Performing abdominal trusts in conscious adults and children older that 1 year -- Procedure 12-2: Relieving a foreign-body airway obstruction in unconscious adults and children older than 1 year -- Procedure 12-3: Performing chest thrust in conscious adults and children older than 1 year -- Procedure 12-4: Clearing the airway in conscious infant -- Procedure 12-5: Clearing the airway in an unconscious infant -- Unit 3: Basic Patient And Resident Care

-- Chapter 13: Patient or resident environment -- Patient or resident unit -- Hospitals -- Long-term care facilities -- Staff work areas -- Assisted-living facilities -- Home health care -- Ensuring comfort -- Cleanliness -- Odor control -- Ventilation -- Room temperature -- Lighting -- Noise control -- Furniture and equipment -- Beds -- Chairs -- Over-bed tables -- Storage units -- Call light and intercom systems -- Privacy curtains and room dividers -- Other equipment -- Personal items -- Chapter 14: Admissions, transfers, and discharges -- Admissions -- Admissions process -- Tactics for making anew patient or resident feel welcome -- Transfers -- Discharges -- Chapter 15: Bedmaking -- Linens and other supplies for bedmaking -- Linens -- Other bedmaking supplies -- Handling of linens -- Standard bedmaking techniques -- Closed (unoccupied) beds -- Occupied beds -- Procedure 15-1: Making an unoccupied (closed) bed -- Procedure 15-2: Making an occupied bed -- Chapter 16: Vital signs, height and weight -- What do vital signs tell us? -- Measuring and recording vital signs -- Body temperature -- Factors affecting the body temperature -- Measuring the body temperature -- Normal and abnormal findings -- Pulse -- Factors affecting the pulse -- Measuring the pulse -- Normal and abnormal findings -- Respiration -- Factors affecting respiration -- Measuring respiration -- Normal and abnormal findings -- Blood pressure -- Factors affecting blood pressure -- Measuring blood pressure -- Normal and abnormal findings -- Height and weight -- Measuring height and weight -- Measuring vital signs in children -- Procedure 16-1: Measuring an oral temperature (glass or electronic thermometer) -- Procedure 16-2: Measuring a rectal temperature (glass or electronic thermometer) -- Procedure 16-3: Measuring an axillary temperature (glass or electronic thermometer) -- Procedure 16-4: Measuring a tympanic temperature (tympanic thermometer) -- Procedure 16-5: Taking a radial pulse -- Procedure 16-6: Taking an apical pulse -- Procedure 16-7: Counting respirations -- Procedure 16-8: Measuring blood pressure -- Procedure 16-9: Measuring height and weight using an upright scale -- Procedure 16-10: Measuring weight using a chair scale -- Procedure 16-11: Measuring

height and weight using a tape measure and a sling scale -- Chapter 17: Comfort and rest -- Physical and emotional benefits of rest and sleep -- Normal sleep -- Factors that can affect sleep -- Nursing assistant's role in promoting rest and sleep -- Pain -- How people respond to pain -- Recognizing and reporting pain -- Treatments for pain -- Nursing assistant's role in managing pain -- Procedure 17-1: Giving a dry heat application with an aquamatic pad -- Procedure 17-2: Giving a moist cold application -- Procedure 17-3: Giving a dry cold application -- Chapter 18: Cleanliness and hygiene -- Benefits of personal hygiene -- Scheduling of routine care -- Assisting with oral care -- Providing oral care for a person with natural teeth -- Providing oral care for a person with dentures -- Providing oral care for an unconscious person -- Assisting with perineal care -- Providing perineal care for female patients and residents -- Providing perineal care for male patients and residents -- Assisting with skin care -- Bathing -- Massage -- Procedure 18-1: Brushing and flossing the teeth -- Procedure 18-2: Providing oral care for a person with dentures -- Procedure 18-3: Providing oral care for an unconscious person -- Procedure 18-4: Providing female perineal care -- Procedure 18-5: Providing male perineal care -- Procedure 18-6: Assisting with a tub bath or shower -- Procedure 18-7: Giving a complete bed bath -- Procedure 18-8: Giving a partial bed bath -- Procedure 18-9: Giving a back massage -- Chapter 19: Grooming -- Assisting with hand and foot care -- Care of the hands -- Care of the feet -- Assisting with dressing and undressing -- Assisting with hair care -- Shampooing the hair -- Styling the hair -- Preventing tangles -- Assisting with shaving -- Assisting men -- Assisting women -- Assisting with the application of make-up -- Procedure 19-1: Assisting with hand care -- Procedure 19-2: Assisting with foot care -- Procedure 19-3: Assisting a person with dressing -- Procedure 19-4: Changing a hospital gown -- Procedure 19-5: Shampooing a person's hair in bed -- Procedure 19-6: Combing a person's hair -- Procedure 19-7: Shaving a person's face -- Chapter 20: Basic nutrition -- Food and how our bodies use it -- Types of nutrients -- Balanced diet -- Factors that affect food choices and eating habits -- Special diets -- Meal time --

Preparing for meal time -- Assisting the person to eat -- Feeding dependent patients and residents -- Measuring and recording food intake -- Other ways of providing fluids and nutrition -- Intravenous (IV) therapy -- Enteral nutrition -- Total parenteral nutrition (TPN, hyperalimentation) -- Fluids and hydration -- Fluid balance -- Offering fluids -- Measuring and recording intake an output -- Procedure 20-1: Feeding a dependent person -- Chapter 21: Assisting with urinary and bowel elimination -- Assisting with elimination -- Elimination equipment -- Promoting normal elimination -- Obtaining urine and stool specimens -- Urinary elimination -- Measuring urine output -- Urinary catheterization -- Urinary incontinence -- Bowel elimination -- Problems with bowel elimination -- Enemas -- Rectal suppositories -- Caring for a person with an ostomy -- Procedure 21-1: Assisting a person with using a bedpan -- Procedure 21-2: Assisting a man with using a urinal -- Procedure 21-3: Collecting a routine urine specimen -- Procedure 21-4: Collecting a midstream(clean catch) urine specimen -- Procedure 21-5: Collecting a stool specimen -- Procedure 21-6: Providing catheter care -- Procedure 21-7: Emptying a urine drainage bag -- Procedure 21-8: Administering a soapsuds enema -- Procedure 21-9: Providing routine ostomy care -- Unit 4: Death And Dying -- Chapter 22: Caring for people who are terminally ill -- Stages of grief -- Wills -- Dying with dignity -- Advance directives -- Hospice care -- Effects of caring for the terminally ill on the caregiver -- Chapter 23: Caring for people who are dying -- Caring for a dying person -- Meeting the dying person's physical needs -- Meeting the dying person's emotional needs -- Care of the family -- Postmortem care -- Procedure 23-1: Providing postmortem care -- Unit 5: Structure And Function Of The Human Body -- Chapter 24: Basic body structure and function -- How is the body organized? -- Cells -- Tissues -- Organs -- Organ systems -- Health and disease -- Categories of disease -- Risk factors for disease -- Chapter 25: Integumentary system -- Structure of the integumentary system -- Skin -- Accessory structures (appendages) -- Function of the integumenary system -- Protection -- Maintenance of fluid balance -- Regulation of body temperature -- Sensation -- Vitamin D

production -- Elimination and absorption -- Effects of aging on the integumentary system -- Changes in physical appearance -- Fragile, dry skin -- Thickening of the nails -- Less efficient temperature regulation -- Disorders of the integumentary system -- Pressure ulcers -- Wounds -- Burns -- Lesions -- Procedure: 25-1: Assisting the nurse with a dressing change -- Chapter 26: Musculoskeletal system -- Structure of the musculoskeletal system -- Skeletal system -- Muscular system -- Function of the musculoskeletal system -- Protection -- Support -- Movement -- Heat production -- Calcium storage -- Production of blood cells -- Effects of aging on the musculoskeletal system -- Loss of bone tissue -- Loss of muscle mass -- Wear and tear on the joints -- Disorders of the musculoskeletal system -- Osteoporosis -- Arthritis -- Muscular dystrophy -- Fractures -- Amputations -- General care measures -- Range-of-motion exercises -- Procedure 26-1: Assisting a person with passive range-of-motion exercises -- Chapter 27: Respiratory system -- Structure of the respiratory system -- Airway -- Lungs -- Function of the respiratory system -- Ventilation -- Gas exchange -- Effects of aging on the respiratory system -- Less efficient ventilation -- Increased risk of respiratory infections -- Disorders of the respiratory system -- Infections -- Asthma -- Chronic obstructive pulmonary disease (COPD) -- Cancer -- Pneumothorax and hemothorax -- Respiratory therapy -- Oxygen therapy -- Mechanical ventilation -- Suctioning -- General care measures -- Observation -- Promoting comfort -- Chapter 28: Cardiovascular system -- Structure of the cardiovascular system -- Blood -- Blood vessels -- Lymphatic system -- Heart -- Function of the cardiovascular system -- Transport -- Regulation -- Protection -- Effects of aging on the cardiovascular system -- Less efficient contraction -- Decreased elasticity of the arteries and veins -- Decreased numbers of blood cells -- Disorders of the cardiovascular system -- Disorders of the blood -- Disorders of the blood vessels -- Disorders of the heart -- Diagnosis of cardiovascular disorders -- Chapter 29: Nervous system -- Structure of the nervous system -- Central nervous system -- Peripheral nervous system -- Function of the nervous system -- Regulation

of the internal environment -- Interaction with the external environment -- Effects of aging on the nervous system -- Slowed conduction times -- Memory changes -- Disorders of the nervous system -- Transient Ischemic Attacks (TIAs) -- Stroke -- Parkinson's disease -- Epilepsy -- Multiple Sclerosis (MS) -- Amyotrophic Lateral Sclerosis (ALS, LOU Gehrig's Disease) -- Head injuries -- Coma and persistent vegetative state -- Spinal cord injuries -- Diagnosis of neurologic disorders -- Chapter 30: Sensory system -- Structure of the sensory system -- General sense -- Touch -- Position -- Pain -- Taste and smell -- Sight -- Structure of the eye -- Function of the eye -- Effects of aging on the eye -- Disorders of the eye -- Caring for eyeglasses, contact lenses, and prosthetic eyes -- Hearing and balance -- Structure of the ear -- Function of the ear -- Effects of aging on the ear -- Disorders of the ear -- Procedure 30-1: Assisting a person with an in-the-ear hearing aid -- Chapter 31: Endocrine system -- Structure of the endocrine system -- Function of the endocrine system -- Pituitary gland -- Pineal gland -- Thyroid gland -- Parathyroid glands -- Thymus gland -- Adrenal glands -- Pancreas -- Sex glands -- Effects of aging on the endocrine system -- Disorders of the endocrine system -- Pituitary gland disorders -- Thyroid gland disorders -- Adrenal gland disorders -- Diabetes mellitus -- Chapter 32: Digestive system -- Structure of the digestive system -- Digestive tract -- Accessory organs -- Function of the digestive system -- Digestion -- Absorption -- Excretion -- Effects of aging on the digestive system -- Less efficient chewing and swallowing -- Less efficient digestion -- Increased risk for constipation -- Disorders of the digestive system -- Ulcers -- Hernias -- Gallbladder disorders -- Cancer -- Diagnosis of digestive disorders -- Chapter 33: Urinary system -- Structure of the urinary system -- Kidneys -- Ureters -- Bladder -- Urethra -- Function of the urinary system -- Removal of liquid wastes -- Maintenance of homeostasis -- Effects of aging on the urinary system -- Disorders of the urinary system -- Infections -- Neurogenic bladder -- Kidney stones (renal calculi) -- Kidney (rental) failure -- Tumors -- Diagnosis of urinary disorders -- Chapter 34: Reproductive system -- Female reproductive system -- Structure of the female reproductive system -- Function

of the female reproductive system -- Effects of aging on the female reproductive system -- Disorders of the female reproductive system -- Common diagnostic procedures -- Common surgical procedures -- Male reproductive system -- Structure of the male reproductive system -- Function of the male reproductive system -- Effects of aging on the male reproductive system -- Disorders of the male reproductive system -- Common diagnostic procedures -- Sexually transmitted infections -- Types of sexually transmitted infections -- Prevention of sexually transmitted infections -- Unit 6: Special Care Concerns -- Chapter 35: Caring for people with rehabilitation needs -- Rehabilitation and restorative care -- Settings for rehabilitation -- Phases of rehabilitation -- Rehabilitation team -- Types of rehabilitation -- Physical rehabilitation -- Emotional rehabilitation -- Vocational rehabilitation -- Factors affecting the rehabilitation effort -- Nursing assistant's role in rehabilitation and restorative care -- Specific rehabilitation measures -- Integumentary system -- Musculokeletal system -- Cardiovascular system -- Nervous system -- Endocrine system -- Digestive, urinary, and reproductive systems -- Chapter 36: Caring for people with developmental disabilities -- What is a developmental disability? -- Special needs of people with developmental disabilities -- Special education -- Protection of rights -- Emotional and social needs -- Types of developmental disabilities -- Mental retardation -- Down syndrome -- Autism -- Cerebral palsy -- Fragile X syndrome -- Fetal alcohol syndrome -- Spina bifida -- Hydrocephalus -- Caring for a person with a developmental disability -- Communicating with a person with a developmental disability -- Meeting the physical needs of a person with a developmental disability -- Chapter 37: Caring for with mental illness -- Mental illness -- Coping mechanisms -- Defense mechanisms -- Causes and treatment of mental illness -- Types of mental illness -- Anxiety disorders -- Post-traumatic stress disorder (PTSD) -- Depression -- Bipolar disorder (manic depression) -- Schizophrenia -- Substance abuse disorders and addiction -- Eating disorders -- Caring for a person with mental illness -- Listening and observing -- Assisting with activities of daily

living (ADLs) -- Chapter 38: Caring for people with dementia -- What is Dementia? -- Causes of dementia -- Alzheimer's disease -- Vascular dementia -- Lewy body dementia -- Frontotemporal dementia -- Behaviors associated with dementia -- Types of behaviors -- Managing difficult behaviors -- Caring for a person with dementia -- Meeting the physical needs of a person with dementia -- Meeting the emotional needs of a person with dementia -- Caring for the person with late-stage dementia -- Effects on the caregiver of caring for the person with dementia -- Chapter 39: Caring for people with cancer -- What is cancer? -- Types of cancer -- Causes of cancer -- Detection of caner -- Warning signs of cancer -- Routine physical examinations and screening tests -- Treatment of cancer -- Caring for a person with cancer -- Meeting the physical needs of a person with cancer -- Meeting the emotional needs of a person with cancer -- Chapter 40: Caring for people with HIV/AIDS -- What is Aids? -- Who is at risk for HIV/AIDS? -- Global health crisis -- Protection of rights -- Caring for a person with AIDS -- Meeting the physical needs of a person with AIDS -- Meeting the emotional needs of a person with AIDS -- Unit 7: Acute Care -- Chapter 41: Caring for surgical patients -- Care of the pre-operative patient -- Emotional preparation -- Physical preparation -- Care of the post-operative patient -- Preventing complications -- Assisting with positioning -- Assisting with nutrition -- Assisting with elimination -- Assisting with hygiene -- Assisting with walking (ambulation) -- Procedure 41-1: Applying anti-embolism (TED) stockings -- Chapter 42: Caring for mother and newborns -- Antepartum (prenatal) period -- Physical changes in pregnancy -- Routine prenatal care -- Complications during pregnancy -- Meeting the pregnant woman's physical needs -- Meeting the pregnant woman's emotional needs -- Labor and delivery -- Labor -- Delivery -- Immediately following delivery -- Postpartum period -- Care of the mother -- Care of the baby -- Chapter 43: Caring for pediatric patients -- Caring for infants -- Meeting the infant's physical needs -- Meeting the infant's emotional needs -- Meeting the infant's need for safety -- Caring for toddlers -- Meeting the toddler's physical needs -- Meeting the toddler's emotional needs --

Meeting the toddler's need for safety -- Caring for preschoolers -- Meeting the preschooler's physical needs -- Meeting the preschooler's emotional needs -- Meeting the preschooler's needs for safety -- Caring for school-age children -- Meeting the school-age child's physical needs -- Meeting the school-age child's emotional needs -- Meeting the school-age child's need for safety -- Caring for adolescents -- Meeting the adolescent's physical needs -- Meeting the adolescent's emotional needs -- Meeting the adolescent's need for safety -- Child abuse -- Forms of abuse -- Risk factors for child abuse -- Role of the nursing assistant in reporting abuse -- Unit 8: Home Health Care -- Chapter 44: Introduction to home health care -- What is home health care? -- Paying for home health care -- Health care team -- Responsibilities of the home health aide -- Personal care -- Homemaking -- Qualities of the successful home health aide -- Ability to work independently -- Ability to be organized and manage time -- Reliability -- Ability to set professional boundaries -- Chapter 45: Safety and infection control in the home health care setting -- Workplace safety -- Accidents and medical emergencies -- Abusive situations -- Infection control -- Maintaining a sanitary environment -- Using standard precautions -- Personal safety -- Appendix A: Answers to the what did you learn? exercises -- Appendix B: Introduction to the language of health care -- Medical terminology -- Anatomical terms -- Directional terms -- Terms used to describe body cavities -- Terms used to describe the abdominal area -- Abbreviations -- Glossary -- Index. Subjects: Nurses' aides. Nursing. Nurses' Aides. Nursing Care. Notes: Includes bibliographical references and index.

Medical language LCCN: 2012036465 Personal name: Turley, Susan M. Main title: Medical language / Susan M. Turley. Edition: 3rd ed. Published/Created: Upper Saddle River, N.J.: Pearson Education, c2014. Description: xxix, 958, A-24, AK-34, PC-3, I-28 p.: col. ill.; 28 cm. ISBN: 9780133346831 0133346838 LC classification: R123 .T87 2014 Contents: The structure of medical language -- The body in health and disease -- Gastroenterology. Gastrointestinal system -- Pulmonology. Respiratory

system -- Cardiology. Cardiovascular system -- Hematology and immunology. Blood and lymphatic system -- Dermatology. Integumentary system -- Orthopedics. Skeletal system -- Orthopedics. Muscular system -- Neurology. Nervous system -- Urology. Urinary system -- Male reproductive medicine. Male genitourinary system -- Gynecology and obstetrics. Female genital and reproductive system -- Endocrinology. Endocrine system -- Ophthalmology. Eye -- Otolaryngology. Ears, nose, and throat -- Psychiatry -- Oncology -- Radiology and nuclear medicine. Subjects: Terminology as Topic-- Problems and Exercises. Notes: Includes index.

Medical language: Immerse yourself
LCCN: 2015045277 Personal name: Turley, Susan M., author. Main title: Medical language: iImmerse yourself / Susan M. Turley. Edition: Fourth edition. Published/Produced: Upper Saddle River, NJ: Pearson, 2015. Description: p.; cm. ISBN: 9780134318127 0134318129 LC classification: R123 Contents: The structure of medical language -- The body in health and disease -- Gastroenterology. Gastrointestinal system -- Pulmonology. Respiratory system -- Cardiology. Cardiovascular system -- Hematology and immunology. Blood and lymphatic system -- Dermatology. Integumentary system -- Orthopedics. Skeletal system -- Orthopedics. Muscular system -- Neurology. Nervous system -- Urology. Urinary system -- Male reproductive medicine. Male genitourinary system -- Gynecology and obstetrics. Female genital and reproductive system -- Endocrinology. Endocrine system -- Ophthalmology. Eye -- Otolaryngology. Ears, nose, and throat -- Psychiatry -- Oncology -- Radiology and nuclear medicine. Subjects: Terminology as Topic-- Problems and Exercises. Notes: Includes index.

Medical terminology complete!
LCCN: 2011045735 Personal name: Wingerd, Bruce D. Main title: Medical terminology complete! / Bruce Wingerd. Edition: 2nd ed. Published/Created: Boston: Pearson, c2013. Description: xxi, 498, [70] p.: col. ill.; 28 cm. ISBN: 9780132843225 0132843226 0132843226 LC classification: R123 .W527 2013 Contents: Introduction to word

parts and word construction -- Understanding suffixes -- Understanding prefixes -- The human body in health and disease -- The integumentary system -- The skeletal and muscular systems -- Blood and the lymphatic system -- The cardiovascular system -- The respiratory system -- The digestive system -- The urinary system -- Reproductive system and obstetrics -- The nervous system and mental health -- The special senses of sight and hearing -- The endocrine system. Subjects: Medicine-- Programmed Instruction. Terminology as Topic-- Programmed Instruction. Notes: Includes glossary-index.

Medical terminology for health care professionals LCCN: 2013033214 Personal name: Rice, Jane, author. Main title: Medical terminology for health care professionals / Jane Rice, RN, CMA-C, Medical Assisting Program Director, Retired, Georgia Northwestern Technical College, Rome, Georgia. Edition: 8th edition. Published/Produced: Boston: Pearson, [2015] Description: xxii, 841 pages: color illustrations; 28 cm ISBN: 9780133429541 (pbk) 0133429547 (pbk) LC classification: R123 .R523 2015 Contents: Introduction to medical terminology -- Suffixes [LH1] -- Prefixes -- Organization of the body -- Integumentary system -- Skeletal system -- Muscular system -- Digestive system -- Cardiovascular system -- Blood and lymphatic system -- Respiratory system -- Urinary system -- Endocrine system -- Nervous system -- Special senses: the ear -- Special senses: the eye -- Female reproductive system with an overview of obstetrics -- Male reproductive system -- Oncology -- Radiology and nuclear medicine -- Mental health. Subjects: Medicine-- Terminology--English. Anatomy--Terminology-- English. Terminology as Topic. Notes: Preceded by Medical terminology: a word-building approach / Jane Rice. 7th ed. c2012.

Medical terminology: a word-building approach LCCN: 2010049708 Personal name: Rice, Jane. Main title: Medical terminology: a word-building approach / Jane Rice. Edition: 7th ed. Published/Created: Upper Saddle River, NJ: Pearson, c2012. Description: xxii, 770, [69] p.: ill. (chiefly col.); 28 cm. ISBN:

9780132148023 (pbk.) 0132148021 (pbk.) LC classification: R123 .R523 2012 Contents: Introduction to medical terminology -- Suffixes -- Prefixes -- Organization of the body -- Integumentary system -- Skeletal system -- Muscular system -- Digestive system -- Cardiovascular system -- Blood and lymphatic system -- Respiratory system -- Urinary system -- Endocrine system -- Nervous system -- Special senses: the ear -- Special senses: the eye -- Female reproductive system with an overview of obstetrics -- Male reproductive system -- Oncology -- Radiology and nuclear medicine -- Mental health. Subjects: Medicine--Terminology. Human anatomy--Terminology. Medicine--Terminology--English. Anatomy--Terminology--English. Terminology as Topic. Notes: Includes index.

Memmler's structure and function of the human body LCCN: 2015017673 Personal name: Cohen, Barbara J., author. Main title: Memmler's structure and function of the human body / Barbara Janson Cohen, Kerry Hull. Edition: Eleventh edition. Published/Produced: Philadelphia: Wolters Kluwer, [2015] Description: p.; cm. ISBN: 9781496317728 (alk. paper) LC classification: QP36 Variant title: Structure and function of the human body Related names: Hull, Kerry L., author. Preceded by (work): Taylor, Jason J. Memmler's structure and function of the human body. Contents: Organization of the human body -- Chemistry, matter, and life -- Cells and their functions -- Tissues, glands, and membranes -- The integumentary system -- The skeleton: bones and joints -- The muscular system -- The nervous system: the spinal cord and spinal nerves -- The nervous system: the brain and cranial nerves -- The sensory system -- The endocrine system: glands and hormones -- The blood -- The heart -- Blood vessels and blood circulation -- The lymphatic system and immunity -- The respiratory system -- The digestive system -- Metabolism, nutrition, and body temperature -- The urinary system and body fluids -- The male and female reproductive systems -- Development and heredity. Subjects: Anatomy. Physiology. Notes: Preceded by Memmler's structure and function of the human body / Jason James Taylor, Barbara Janson Cohen. 10th ed. c2013. Includes

bibliographical references and index.

Memmler's the human body in health and disease / Barbara Janson Cohen; consulting editorsauthors, Jason James Taylor, Kerry L. Hull. LCCN: 2011048302 Personal name: Cohen, Barbara J. Main title: Memmler's the human body in health and disease / Barbara Janson Cohen; consulting editors/authors, Jason James Taylor, Kerry L. Hull. Edition: 12th ed. Published/Created: Philadelphia: Wolters Kluwer Health/Lippincott Williams and Wilkins, c2013. Description: xxxi, 640 p.: col. ill.; 28 cm. + 1 DVD-ROM (4 3/4in.) ISBN: 9781609139056 (soft cover) 9781609139070 (hardcover) LC classification: QP34.5 .M48 2013 Variant title: Human body in health and disease Related names: Taylor, Jason J. Hull, Kerry L. Memmler, Ruth Lundeen. Contents: Organization of the human body -- Chemistry, matter, and life -- Cells and their functions -- Tissues, glands, and membranes -- Disease and disease-producing organisms -- The skin in health and disease -- The skeleton: bones and joints -- The muscular system -- The nervous system: the spinal cord and spinal nerves -- The nervous system: the brain and cranial nerves -- The sensory system -- The endocrine system: glands and hormones -- The blood -- The heart and heart disease -- Blood vessels and blood circulation -- The lymphatic system and lymphoid tissue -- Body defenses, immunity, and vaccines -- The respiratory system -- The digestive system -- Metabolism, nutrition, and body temperature -- Body fluids -- The urinary system -- The male and female reproductive systems -- Development and birth -- Heredity and hereditary diseases. Subjects: Physiology. Anatomy. Pathology. Notes: Includes index.

Memmler's the human body in health and disease. LCCN: 2014021555 Personal name: Cohen, Barbara J., author. Main title: Memmler's the human body in health and disease. Edition: 13th edition / Barbara Janson Cohen, Kerry L. Hull. Published/Produced: Philadelphia: Wolters Kluwer, [2015] Description: xxxi, 665 pages, 16 unnumbered pages of plates, unnumbered leaves of transparent overlays: color illustrations; 28 cm ISBN: 9781451192803 (pbk.: alk. paper) 9781451193749 (hbk:

alk. paper) 1451193742 (hbk: alk. paper) LC classification: QP34.5 .M48 2015 Variant title: Human body in health and disease Related names: Hull, Kerry L., author. Contents: Organization of the human body -- Chemistry, matter, and life -- Cells and their function -- Tissues, glands, and membranes -- Disease and disease-producing organisms -- The integumentary system -- The skeleton: bones and joints -- The muscular system -- The nervous system: the spinal cord and the spinal nerves -- The nervous system: the brain and cranial nerves -- The sensory system -- The endocrine system: glands and hormones -- The blood -- The heart and heart disease -- Blood vessels and blood circulation -- The lymphatic system and lymphoid tissue -- Immunity -- The respiratory system -- The digestive system -- Metabolism, nutrition, and body temperature -- Body fluids -- The urinary system -- The male and female reproductive systems -- Development and birth -- Heredity and hereditary diseases. Subjects: Physiological Phenomena. Anatomy. Pathology. Notes: Includes bibliographical references and index.

Mosby's dictionary of medicine, nursing and health professions. LCCN: 2012028343 Main title: Mosby's dictionary of medicine, nursing and health professions. Edition: 9th ed. Published/Created: St. Louis, Mo.: Elsevier/Mosby, c2013. Description: xiv, A-43, 1989 p.: ill. (chiefly col.); 26 cm. ISBN: 9780323074032 (hardcover: alk. paper) LC classification: R121 .M89 2013 Variant title: Dictionary of medicine, nursing and health professions Mosby's dictionary of medicine, nursing, and health professions Related names: Mosby, Inc. Contents: Color atlas of human anatomy -- Skeletal system -- Muscular system -- Circulatory system -- Endocrine system -- Lymphatic system -- Nervous system -- Respiratory system -- Digestive system -- Reproductive system -- Urinary system -- Special senses -- Vocabulary. Subjects: Medicine--Dictionaries. Nursing--Dictionaries. Medicine--Dictionary--English. Allied Health Occupations--Dictionary--English. Nursing--Dictionary--English.

Mosby's medical dictionary LCCN: 2012028208 Main title: Mosby's medical dictionary / [editor, Marie T. O'Toole]. Edition: 9th ed. Published/Created: St. Louis,

Mo.: Elsevier/Mosby, c2013. Description: xiv, A1-A43, 1921 p.: ill. (chiefly col.); 26 cm. ISBN: 9780323085410 (hardcover: alk. paper) LC classification: R121 .M89 2013 Variant title: Medical dictionary Related names: O'Toole, Marie T. Contents: Color atlas of human anatomy -- Skeletal system -- Muscular system -- Circulatory system -- Endocrine system -- Lymphatic system -- Nervous system -- Respiratory system -- Digestive system -- Reproductive system -- Urinary system -- Special senses -- Vocabulary. Subjects: Medicine--Dictionaries. Medicine--Dictionary--English.

Nurses' handbook of health assessment LCCN: 2013024190 Main title: Nurses' handbook of health assessment / [edited by] Janet R. Weber. Edition: Eighth edition. Published/Produced: Philadelphia: Wolters Kluwer/Lippincott Williams and Wilkins Health, [2014] Description: 788 pages: color illustrations; 19 cm. ISBN: 9781451142822 (alk. paper) LC classification: RT48 .N863 2014 Related names: Weber, Janet, editor. Contents: Obtaining a nursing health history -- Collecting subjective and objective data -- Performing physical assessment skills -- Assessing psychosocial, cognitive, and moral development -- Assessing mental status and substance abuse -- Assessing general status and vital signs -- Assessing pain: the 5th vital sign -- Assessing for violence -- Assessing nutritional status -- Assessing skin, hair, and nails -- Assessing head and neck -- Assessing eyes -- Assessing ears -- Assessing mouth, throat, nose, and sinuses -- Assessing thorax and lungs -- Assessing breasts and lymphatic system -- Assessing heart and neck vessels -- Assessing peripheral vascular system -- Assessing abdomen -- Assessing musculoskeletal system -- Assessing neurological system -- Assessing male genitalia and rectum -- Assessing female genitalia and rectum -- Assessing childbearing women -- Assessing newborns and infants -- Assessing older adults. Subjects: Nursing Assessment--methods--Handbooks. Medical History Taking--methods--Handbooks. Physical Examination--methods--Handbooks. Notes: Includes bibliographical references (pages 757-769) and index.

Ross and Wilson anatomy and physiology in health and illness

LCCN: 2014004368 Personal name: Waugh, Anne, author. Main title: Ross and Wilson anatomy and physiology in health and illness / Anne Waugh, BSc(Hons), MSc, CertEd, SRN, RNT, FHEA, Senior Teaching Fellow and Director of Academic Quality, School of Nursing, Midwifery and Social Care, Edinburgh, Napier University, Edinburgh, UK, Allison Grant, Lecturer, Division of Biological and Biomedical Sciences, Glasgow Caledonian University, Glasgow, UK; illustrations by Graeme Chambers. Edition: 12th edition. Published/Produced: Edinburgh; New York: Churchill Livinstone Elsevier, [2014] ©2014 Description: xii, 509 pages: color illustrations; 28 cm ISBN: 9780702053252 (pbk.) 0702053252 (pbk.) 9780702053269 (International ISBN) 0702053260 (International ISBN) LC classification: RT69 .W384 2014 Variant title: Anatomy and physiology in health and illness Related names: Grant, Allison (Allison Wynn), 1961- author. Contents: Introduction to the human body -- Introduction to the chemistry of life -- The cells, tissues and organisation of the body -- The blood -- The cardiovascular system -- The lymphatic system -- The nervous system -- The special senses -- The endocrine system -- The respiratory system -- Introduction to nutrition -- The digestive system -- The urinary system -- The skin -- Resistance and immunity -- The musculoskeletal system -- Introduction to genetics -- The reproductive systems. Subjects: Anatomy--Nurses' Instruction. Physiology--Nurses' Instruction. Notes: Includes bibliographical references (page 481) and index.

Seidel's physical examination handbook. LCCN: 2015413987 Personal name: Ball, Jane (Jane W.) Uniform title: Mosby's physical examination handbook Main title: Seidel's physical examination handbook. Edition: Eighth edition / Jane W. Ball, RN, DrPH, CPN, Trauma Systems Consultant, American College of Surgeons, Gaithersburg, Maryland [and four others]; reviewer Susan D. Rymer, MSN, RN, Assistant Professor, School of Nursing, Bellin College, Green Bay, Wisconsin. Published/Produced: St. Louis, Missouri: Elsevier, [2015] Description: viii, 328 pages: illustrations (chiefly color); 20 cm ISBN: 9780323169530 (pbk) LC classification: RC76 .M64 2015

Variant title: Physical examination handbook. Related names: Seidel, Henry M. Contents: The history --Vital signs and pain assessment -- Mental status -- Nutrition and growth and measurement -- Skin, hair, and nails -- Lymphatic system -- Head and neck -- Eyes -- Ears, nose, and throat -- Chest and lungs -- Heart -- Blood vessels -- Breasts and axillae -- Abdomen -- Female genitalia -- Male genitalia -- Anus, rectum, and prostate -- Musculoskeletal system -- Neurologic system -- Head-to-toe examination: adult -- Age-specific examination: infants, children, and adolescents -- Age-spectific examination: Special populations and older adults -- The healthy female evaluation -- Sports participation evaluation -- Reporting and recording. Subjects: Physical diagnosis--Handbooks, manuals, etc. Notes: Revision of: Mosby's physical examination handbook / Henry M. Seidel ... [et al.]. 7th ed. 2011. Includes bibliographical references (pages 305-311) and index.

Structure and function of the body LCCN: 2011030968 Personal name: Thibodeau, Gary A., 1938- Main title: Structure and function of the body / Gary A. Thibodeau, Kevin T. Patton. Edition: 14th ed. Published/Created: St. Louis, Mo.: Elsevier/Mosby, c2012. Description: xix, 495, [59] p.: col. ill.; 26 cm. + 1 CD-ROM (4 3/4 in.) ISBN: 9780323077217 (hardcover: alk. paper) 0323077218 (hardcover: alk. paper) 9780323077224 (pbk.: alk. paper) 0323077226 (pbk.: alk. paper) LC classification: QP34.5 .T5 2012 Variant title: Structure and function of the body Related names: Patton, Kevin T. Anthony, Catherine Parker, 1907- Structure and function of the body. Contents: An introduction to the structure and function of the body -- Chemistry of life -- Cells and tissues -- Organ systems of the body -- The integumentary system and body membranes -- The skeletal system -- The muscular system -- The nervous system -- The senses -- The endocrine system -- Blood -- The cardiovascular system -- The lymphatic system and immunity -- The respiratory system -- The digestive system -- nutrition and metabolism -- The urinary system -- Fluid and electrolyte balance -- Acid-base balance -- The reproductive systems -- Growth and development. Subjects: Human

physiology--Textbooks. Human anatomy--Textbooks. Anatomy. Physiology. Notes: Includes index. Includes bibliographical references and index.

The biology book: from the origin of life to epigenetics, 250 milestones in the history of biology LCCN: 2015304935 Personal name: Gerald, Michael C. Main title: The biology book: from the origin of life to epigenetics, 250 milestones in the history of biology / Michael C. Gerald, with Gloria E. Gerald. Published/Produced: New York, NY: Sterling, [2015] ©2015 Description: 526 pages: color illustrations; 22 cm ISBN: 9781454910688 (hardcover) 1454910682 (hardcover) LC classification: QH305 .G46 2015 Related names: Gerald, Gloria. Summary: From the emergence of life, to Leewenhoek's microscopic world, to GMO crops, The Biology Book presents 250 landmarks in the most widely studied scientific field. Brief, engaging, and colorfully illustrated synopses introduce readers to every major subdiscipline, including cell theory, genetics, evolution, physiology, thermodynamics, molecular biology, and ecology. With information on such varied topics as paleontology, pheromones, nature vs. nurture, DNA fingerprinting, bioenergetics, and so much more, this lively collection will engage everyone who studies and appreciates the life sciences. -- Source other than Library of Congress. Contents: Origin of life -- Last universal common ancestor -- Prokaryotes -- Algae -- Eukaryotes -- Fungi -- Arthropods -- Medulla: the vital brain -- Fish -- Land plants -- Devonian Period -- Insects -- Plant defenses against herbivores -- Amphibians -- Seeds of success -- Reptiles -- Gymnosperms -- Dinosaurs -- Mammals -- Birds -- Angiosperms -- Primates -- Amazon rainforest -- Neanderthals -- Anatomically modern humans -- Plant-derived medicines -- Wheat: the staff of life -- Agriculture -- Domestication of animals -- Coral reefs -- Rice cultivation -- Mummification -- Animal navigation -- Four humors -- Aristotle's The history of animals -- Animal migration -- Botany -- Pliny's Natural history -- Skeletal system -- Pulmonary circulation -- Leonardo's human anatomy -- Sense of hearing -- Vesalius's De humani corporis fabrica -- Tobacco -- Metabolism -- Scientific method -- Harvey's De motu cordis --

Mechanical philosophy of Descartes -- Placenta -- Lymphatic system -- Blood cells -- Refuting spontaneous generation -- Phosphorus cycle -- Egotism and witchcraft -- Leeuwenhoek's microscopic -- Spermatozoa -- Miasma theory -- Circadian rhythms -- Blood pressure -- Linnean classification of species -- Cerebrospinal fluid -- Regeneration -- Theories of germination -- Artificial selection (selective breeding) -- Animal electricity -- Gas exchange -- Nervous system communication -- Paleontology -- Population growth and food supply -- Lamarckian inheritance -- Germ-layer theory of development -- Cell nucleus -- Darwin and the voyages of the Beagle -- Anatomy Act of 1832 -- Human digestion -- Fossil record and evolution -- Nitrogen cycle and plant chemistry -- Cell theory -- Plant nutrition -- Urine formation -- Apoptosis (programmed cell death) -- Venoms -- Homology versus analogy -- Photosynthesis -- Optical isomers -- Testosterone -- Trichromatic color vision -- Homeostatis -- The liver and glucose metabolism -- Microbial fermentation -- Darwin's theory of natural selection -- Ecological interactions -- Invasive species -- Localization of cerebral function -- Biological mimicry -- Mendelian inheritance -- Ontogeny recapitulates phylogeny -- Hemoglobin and hemocyanin -- Deoxyribonucleic acid (DNA) -- Sexual selection -- Coevolution -- Nature versus nurture -- Biosphere -- Meiosis -- Biogeography -- Marine biology -- Enzymes -- Phototropism -- Mitosis -- Thermoreception -- Innate immunity -- Germ plasm theory of heredity -- Eugenics -- Gram stain -- Negative feedback -- Germ theory of disease -- Animal coloration -- Neuron doctrine -- Endotoxins -- Global warming -- Adaptive immunity -- Associative learning -- Ehrlich's side-chain theory -- Malaria-causing protozoan parasite -- Viruses -- Ecological succession -- Animal locomotion -- Genetics rediscovered -- Ovaries and female reproduction -- Blood types -- Tissue culture -- Secretin: the first hormone -- Dendrochronology -- Blood clotting -- Radiometric dating -- Probiotics -- Why does the heart beat? -- Hardy-Weinberg equilibrium -- Genes on chromosomes -- Cancer-causing viruses -- Continental drift -- Vitamins and bereberi -- Thyroid gland and metamorphosis -- X-ray

crystallography -- Bacteriophages -- Biotechnology -- Neurotransmitters -- Insulin -- Inborn errors of metabolism -- Embryonic induction -- Timing fertility -- Mitochondria and cellular respiration -- "The monkey trial" -- Population ecology -- Food webs -- Insect dance language -- Antibiotics -- Progesterone -- Osmoregulation in freshwater and marine fish -- Electron microscope -- Imprinting -- Factors affecting population growth -- Stress -- Allometry -- Evolutionary genetics -- Coelacanth: "the living fossil" -- Action potential -- One gene-one enzyme hypothesis -- Biological species concept and reproductive isolation -- Arabidopsis: a model plant -- DNA as carrier of genetic information -- Green revolution -- Bacterial genetics -- Reticular activating system -- Phylogenetic systematics -- The immortal HeLa cells -- Cloning (nuclear transfer) -- Amino acid sequence of insulin -- Pattern formations in nature -- Plasmids -- Nerve growth factor -- Miller-Urey experiment -- The double helix -- REM sleep -- Acquired immunological tolerance and organ transplantation -- Sliding filament theory of muscle contraction -- Ribosomes -- Lysosomes -- Prenatal genetic testing -- DNA polymerase -- Second messengers -- Protein structures and folding -- Bioenergetics -- Central dogma of molecular biology -- Bionics and cyborgs -- Pheromones -- Energy balance -- Chimpanzee use of tools -- Cellular senescence -- Cracking the genetic code for protein biosynthesis -- Operon model of gene regulation -- Thrifty gene hypothesis -- Silent spring -- Hybrids and hybrid zones -- Brain lateralization -- Animal altruism -- Optimal foraging theory -- Bacterial resistance to antibiotics -- Endosymbiont theory -- Multi-store model of memory -- Hypothalamic-pituitary axis -- Systems biology -- Cellular determination -- Cell cycle checkpoints -- Punctuated equilibrium -- Sustainable development -- Parental investment and sexual selection -- Lucy -- Cholesterol metabolism -- Sense of taste -- Monoclonal antibodies -- Sociobiology -- Cancer-causing genes -- Bioinformatics -- In Vitro fertilization (IVF) -- Biological magnification -- Can living organisms be patented? -- Genetically modified crops -- HIV and AIDS -- Polymerase chain reaction -- DNA fingerprinting -- Genomics -- Mitochondrial Eve -- Depletion

of the ozone layer -- Domains of life -- Sense of smell -- Leptin: the thinness hormone -- Skin color -- Human Genome Project -- Protist taxonomy -- Induced pluripotent stem cells -- Vital mutations and pandemics -- Deepwater Horizon (BP) oil spill -- Translational biomedical research -- Albumin from rice -- Human Microbiome Project - Epigenetics -- American chestnut tree blight -- De-extinction -- Oldest DNA and human evolution. Subjects: Biology--History. Biology. Form/Genre: History. Notes: Includes bibliographical references (pages 514-522) and index. Series: Sterling Milestones series Sterling Milestones series.

The cardiac lymphatic system: an overview LCCN: 2013935496 Main title: The cardiac lymphatic system: an overview / Ganga Karunamuni, editor. Published/Produced: New York: Springer, [2013] Description: x, 184 pages: illustrations; 24 cm. ISBN: 9781461467731 (hdbk.: alk. paper) 146146773X (hdbk.: alk. paper) LC classification: QM197 .C37 2013 Related names: Karunamuni, Ganga, editor of compilation. Subjects: Cardiovascular Diseases--complications. Lymphatic System--physiopathology. Notes: Includes bibliographical references and index.

The human body in health and disease LCCN: 2012046273 Personal name: Patton, Kevin T. Main title: The human body in health and disease / Kevin T. Patton, Gary A. Thibodeau. Edition: 6th ed. Published/Created: St. Louis, MO: Elsevier/Mosby, c2014. Description: xxviii, 770 p.: ill. (some col.); 28 cm. ISBN: 9780323101233 (hardcover: alk. paper) 9780323101240 (pbk.: alk. paper) LC classification: QP34.5 .T495 2014 Variant title: Human body in health and disease Related names: Thibodeau, Gary A., 1938- Thibodeau, Gary A., 1938- Human body in health and disease. Contents: An introduction to the structure and function of the body -- Chemistry of life -- Cells -- Tissue -- Organ systems of the body -- Mechanisms of disease -- The integumentary system and body membranes -- The skeletal system -- The muscular system -- The nervous system -- The senses -- The endocrine system -- Blood -- The heart -- The circulation of the blood -- The lymphatic system and immunity -- The respiratory system -- The

digestive system -- Nutrition and metabolism -- The urinary system -- Fluid and electrolyte balance -- Acid-base balance -- The reproductive systems -- Growth and development -- Genetics and genetic diseases. Subjects: Physiological Phenomena. Anatomy. Pathology. Notes: Rev. ed. of: The human body in health and disease / Gary A. Thibodeau, Kevin T. Patton. 5th ed. c2010. Includes bibliographical references and index.

Ultrastructure atlas of human tissues
LCCN: 2013042704 Personal name: Hossler, Fred E., author. Main title: Ultrastructure atlas of human tissues / Fred E. Hossler, PhD, Professor Emeritus of Biomedical Sciences, J.H. Quillen College of Medicine, East Tennessee State University, Johnson City, Tennessee, USA. Published/Produced: Hoboken, Jersey: Wiley-Blackwell, [2014] Description: xiv, 952 pages: illustrations; 29 cm ISBN: 9781118284537 (cloth) 1118284534 (cloth) LC classification: QM557 .H673 2014 Summary: "The Ultrastructure Atlas of Human Tissues presents a variety of scanning and transmission electron microscope images of the major systems of the human body. Photography with the electron microscope records views of the intricate substructures and micro-designs of objects and tissues, and reveals details within them inaccessible to the naked eye or light microscope. Many of these views have significance in understanding normal structure and function, as well as disease processes. The Ultrastructure Atlas of Human Tissue offers a unique and comprehensive look at the structure and function of tissues at the sub-cellular and molecular level, an important perspective in the understanding and combating disease"-- Provided by publisher. Contents: Machine generated contents note: Cellular Organelles and Surface Specializations Blood Cells -- Connective Tissues -- Muscle Tissues -- Nerve Tissues --Cardiovascular System -- Lymphatic System -- Gastrointestinal Tract -- Liver (rat) and Gall Bladder -- Pancreas -- Respiratory Tract -- Urinary Tract -- Eye -- Ear -- Male Reproductive System -- Female Reproductive System Subjects: Histology--Atlases. Tissues--ultrastructure--Atlases. Microscopy, Electron--Atlases. Notes: Includes bibliographical references and index. Additional formats: Online version:

Hossler, Fred E., author. Ultrastructure atlas of human tissues Hoboken,

Using medical terminology LCCN: 2012026124 Personal name: Nath, Judi Lindsley. Main title: Using medical terminology / Judi L. Nath. Edition: 2nd ed. Published/Created: Philadelphia: Wolters Kluwer Health/Lippincott Williams and Wilkins, c2013. Description: xxxviii, 1234 p.: col. ill.; 29 cm. ISBN: 9781451115833 (pbk.) LC classification: R123 .N32 2013 Summary: "Using Medical Terminology, 2e is written to teach the language of medicine in an engaging and meaningful way by chunking information into manageable blocks of text and immersing learners into the language of medicine. By using medical terminology in context, students will be prepared to enter the workforce. The number of exercises has expanded greatly, providing more opportunity to practice and review. The design for the second edition has been improved to make the text more appealing and much easier to use. The overall writing has been made even more student-friendly to help comprehension of medical terms without getting lost in scientific writing. The art program has been improved so that figure labels are less cluttered and include only those medical terms introduced in the chapter. The number of photographs has also increased significantly. Two new chapters, Oncology and Gerontology, have been included. In addition, former chapters 5 and 6, Skeletal System and Articulations, have been combined into one cohesive chapter, Skeletal System: Bones and Joints."-- Provided by publisher. Contents: Machine generated contents note: Chapter 1. Introduction to Medical Terminology Chapter 2. Anatomical and Physiological Terminology Chapter 3. Radiology and Nuclear Medicine Chapter 4. Integumentary System Chapter 5. Skeletal System: Bones and Joints Chapter 6. Muscular System Chapter 7. Nervous System Chapter 8. Special Senses Chapter 9. Endocrine System Chapter 10. Blood Chapter 11. Cardiovascular System Chapter 12. Respiratory System Chapter 13. Lymphatic System and Immunity Chapter 14. Digestive System Chapter 15. Urinary System Chapter 16. Reproductive Systems Chapter 17. Pregnancy, Human Development, and Child Health Chapter 18. Mental Health

Chapter 19. Pharmacology Chapter 20. Oncology Chapter 21. Gerontology. Subjects: Terminology as Topic-- Problems and Exercises. Notes: Includes index.

Visual essentials of anatomy and physiology LCCN: 2011040690 Main title: Visual essentials of anatomy and physiology / Frederic H. Martini ... [et al.]; with Claire W. Garrison, Kathleen Welch. Published/Created: Boston: Pearson, c2013. Description: 1 v. (various pagings): col. ill.; 28 cm. ISBN: 9780321780775 0321780779 LC classification: QM32 .V57 2013 Variant title: Visual essentials of anatomy and physiology Related names: Martini, Frederic. Contents: An introduction to anatomy and physiology -- Chemical level of organization -- Cells and tissues -- The integumentary system -- The skeletal system -- The muscular system -- Neural tissue and the central nervous system -- The peripheral and autonomic nervous systems -- The general and special senses -- The endocrine system -- Blood and blood vessels -- The heart and cardiovascular function -- The lymphatic system and immunity -- The respiratory system -- The digestive system -- Nutrition and metabolism -- The urinary system and acid-base balance -- The reproductive system -- Development and inheritance. Subjects: Anatomy--Problems and Exercises. Physiological Phenomena--Problems and Exercises. Notes: Includes index.

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